MEETING

STATE OF CALIFORNIA

AIR RESOURCES BOARD

AIR QUALITY ADVISORY COMMITTEE

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10:00 A.M.

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APPEARANCES

ADVISORY COMMITTEE MEMBERS

Mr. Michael Kleinman, Ph.D., Chairperson

Mr. William Adams, Ph.D.

Ms. Lauraine Chestnut, Ph.D.

Mr. Ralph Delfino, M.D., Ph.D.

Ms. Michelle V. Fannuchi, Ph.D.

Mr. Peter Green, Ph.D.

Ms. S. Katharine Hammond, Ph.D.

Mr. Arnold Platzker, M.D.

Mr. Russell Sherwin, M.D.

AIR RESOURCES BOARD REPRESENTATIVES

Mr. Richard Bode, Chief, Health and Exposure Assessment Branch

Dr. Deborah Drechsler, Research Division

Ms. Leslie Krinsk, Senior Staff Counsel

Dr. Linda Smith, Manager, Health & Exposure Assessment Branch

Mr. Ken Stroud, Chief, Air Quality Surveillance Branch

Dr. Tony Van Curen, Research Division

APPEARANCES CONTINUED

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT
REPRESENTATIVES

Dr. Melanie Marty, Manager, Air Toxicology and Epidemiology Section

Dr. Bart Ostro, Supervisor, Air Toxicology and Epidemiology Section

ALSO PRESENT

Ms. Bonnie Holmes-Gen, American Lung Association of California

Dr. Harold Farber, Kaiser Permanente

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PROCEEDINGS

CHAIRPERSON KLEINMAN: Good morning, everybody.

I'd like to call this meeting of the Air Quality Advisory Committee to order.

And I believe everybody's had a chance to find a copy of the agenda. I don't know if any of you had a chance to look outside this morning around 8:30. And you look out over the marina towards San Francisco, and there was this huge rainbow right over the bay, so I think it bodes well for the proceedings.

And I don't think I've seen the air cleaner here in the number of times I've been up here, so I think we're off to a good start.

With that, I'd like to introduce Richard Bode from the Air Resources Board who will give us a brief introduction.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE:

Great. Thank you, Mike.

My name is Richard Bode. And I'm with the Air Resources Board. And I'm Chief of the Health and Exposure Assessment Branch. And my group is working with the Office of the Environmental Health Hazard Assessment who has been responsible for the review of the California's ambient air quality standard for ozone and the reason for our meeting today.

I'll have to get as close as I can to this thing.

Let me just go on that of course today's meeting is this is the meeting of the Air Quality Advisory Committee, which will do the scientific peer review of our draft staff report.

(Thereupon an overhead presentation was presented as follows.)

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: We have 10 members of our Air Quality Advisory Committee, which is being chaired by Dr. Michael Kleinman.

Mike, would you like to start off by kind of an introduction of the committee members.

CHAIRPERSON KLEINMAN: I think that's a good idea. What I'd like to do is just go around the table and each member can identify themselves, their affiliation and their area of expertise. And this is the first time that the entire committee has actually met face to face. So for me it's a great pleasure to welcome members who have not participated in this before.

I wanted to just sort of, at the outset, kind of lay down a bit of a framework that the purpose of this committee, as Richard said, is to evaluate the scientific basis which is used by the staff of OEHHA and ARB to make -- to prepare the document. They've done a very comprehensive review of the literature.

Unfortunately, as is in every case, it's impossible to do a complete cataloging of all of the scientific information relevant to ozone. The thousands of papers developed and published since the last ozone review. And this is -- it was a formidable task. And I'd just like to start out by congratulating the staff's of the agencies for producing a document that is relatively comprehensive and actually even is readable.

There are some areas that I think as anybody will mention that can use some additional elucidation. But by and large, they've done a very good job of doing a formidable database.

So with that, I'd like to have each member of the Committee identify themselves. And I'll start out. I'm Michael Kleinman. I'm a professor of Community and Environmental Medicine at UC Irvine. My area of study has involved human exposure studies with ozone, animal exposure studies with ozone, and the toxicology of ambient air pollutants in general.

I'd like to pass this on.

ADVISORY COMMITTEE MEMBER HAMMOND: I'm Kathy Hammond. And I'm a professor of Environmental Health Science at the University of California Berkeley, School of Public Health. I'm a chemist and an industrial hygienist. And my area of research is exposure assessment

for epidemiologic studies.

ADVISORY COMMITTEE MEMBER SHERWIN: I'm Russ Sherwin. I'm a pathology professor at the University of Southern California. I have 2 areas in which I work. One is animal studies with ozone and nitrogen dioxide. And the other one is human pathology. We have done a number of studies finding out what the basic pathology is of quote "normal" young people. And this has been an area where we have tried to make correlations between air pollution and the kind of lesions that we've been seeing actually in humans.

ADVISORY COMMITTEE MEMBER ADAMS: Hi. I'm Bill Adams, Professor Emeritus from UC Davis in exercise biology. I've done quite a number of human exposures involving exercise in both short-term, 1- to 2-hour time intervals as well as prolonged exposure, 6.6 hours. I've now moved to Albuquerque, and I find that I'm taking retirement far too seriously.

(Laughter.)

ADVISORY COMMITTEE MEMBER PLATZKER: I'm Arnold Platzker. I'm a neonatologist and a pediatric pulmonologist and a professor USC, and the Children's Hospital Los Angeles an adjunct professor at UCLA. My interests have always been the impact of early lung injury on later lung development. And we've studied premature

infants early aspiration HIV over 7 years in infants born to mothers infected with HIV. And we are more interested as well in various forms of interstitial lung disease, especially those of immunologic basis.

Glad to be here.

ADVISORY COMMITTEE MEMBER FANUCCHI: Hi. My name is Michelle Fanucchi. I'm a professional researcher at UC Davis in the School of Veterinary Medicine. My areas of interest are post-natal lung toxicology, specifically with hazardous air pollutants. And I also work with a nonhuman primate model of ozone toxicity in post-natal animals.

ADVISORY COMMITTEE MEMBER CHESTNUT: I'm Laurie Chestnut and I'm an economist with Stratus Consulting in Colorado. And my area of expertise is benefits assessment, quantitative methods assessment of pollution control.

ADVISORY COMMITTEE MEMBER DELFINO: I'm Ralph Delfino an associate professor at UC Irvine. And I began my research doing time series studies of air pollution health effects and expanded to look at epidemiologic -- other epidemiologic designs, and have focused on asthmatic children and health effects of ambient pollutants on lung function symptoms and other outcomes. And have moved on as well to health effects of air pollutants on cardiovascular disease.

ADVISORY COMMITTEE MEMBER GREEN: I'm Peter Green a professional researcher at UC Davis in the Department of Civil and Environmental Engineering. And I work on a variety of air quality issues, including aerosols, ozone reaction products, sources of ozone precursors and others.

CHAIRPERSON KLEINMAN: Thank you very much. As you can see, we have a very broad group of panel members in terms of areas of expertise. And I believe it covers very adequately the gamut of issues that are raised by the document that's been prepared.

In terms of meeting logistics -- you've probably all seen the agenda -- we have tried, to the best of our ability, to shorten the presentation times by the staff because everyone has presumably read the document or much of the document as interested them. And therefore, we'll just be covering highlights.

Obviously, these presentations are not intended to be total comprehensive. So if there are questions, we'll certainly be able to entertain those. We wanted to allow adequate time possibly even a little bit of time this afternoon, and certainly a major piece of time tomorrow morning for public comments. We feel that's an important part of this process. We wanted to allow enough time for people who have requested time to present issues to have that opportunity.

Most of the people who will be speaking have also provided written comments. And I'd certainly like to make sure that it's understood that what should be presented in the public oral comments are things that either were not adequately addressed in the staff response, because the staff has responded to all written comments at this point, or new information.

And we'll allow some brief time for that. And I will have to use the prerogative of the chair to shorten discussions, if necessary, because I do want to make sure everybody who's requested time does have some time to make their points.

In terms of the Committee itself, we will have a separate room. We're not trying to be snobbish, but we do need -- as I said, we didn't have very much time for individual discussions about the issues, and we do want to make time both at lunch and at dinner tonight for the committee to have time to interact and for me to gather enough information that by tomorrow we will have our consensus opinions.

So that's really all I want to say about meeting logistics. I think that there are -- is Sue -- no. --

Well, I think most people of probably located where the restrooms or washrooms are. The restaurant is in the building, and so there shouldn't be any about if it

starts raining, you don't have to get wet.

And other than that I'd like to again turn this over to Richard for any other comments about the logistics or the agenda.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: Great. Thank you, Dr. Kleinman. I'd just like to point out on the agenda that we have handouts of the agenda for those attending. Hopefully, all the committee members have a copy. If you need some, let us know, and I'll get you a copy of anything we have.

Our meeting is broken into 2 days that will have a short overview of the discussion of the staff report immediately. And then we'll go into -- the rest of the day will be spent on reviews by the Committee itself, the Committee members.

As Dr. Kleinman pointed out that tonight we have a special room for the committee members to eat dinner and actually confer in private, and have the time. Then tomorrow morning will be spent on public comments. The first being a summary by staff of written comments and responses to comments. Followed by an extended oral public comment period. As Dr. Kleinman pointed out, those oral comments should be confined to new information that wasn't included in the written comments, so that everyone has enough time.

And I would say for those that are attending now too, there's a sign-up sheet. If you want to comment tomorrow, and you haven't already done so, make sure you sign up with Sue Wyman in the back of the room.

And then after lunch again we have the private room for the committee tomorrow at lunch time to confer again. And following that, we'll hear the, I guess, discussions of AQAC findings, Committee findings.

So with that, if there are no other questions, I will start off the initial staff presentation. Just to let the Committee know that before you is a draft staff report that was put together by staff from both the Air Resources Board and Office of Environmental Health Hazard Assessment. Dr. Deborah Drechsler was the lead person for the ARB and Dr. Bart Ostro was the lead person for OEHHA.

The staff report actually was released in June of 2004 to the public for review. And approximately a month after that we also released a second document, which was a draft chapter 10, which dealt with just the health benefits for meeting the new recommended standard for ozone.

That chapter, the health benefits chapter, does not contain the basis for supporting the recommendation for the standard, but only -- its purpose was to illustrate what health benefits we could expect if we now

met the new recommended standard.

We did have, as I said, a public comment period. We ended it on September 1st. We've taken those comments and staff has responded in writing to those comments. The draft staff report, as well as the Chapter 10 Health Benefits chapter and all written public comments and staff responses were presented to the Committee for review back in November.

And so actually that is our charge today. And with that, I will let Dr. Drechsler begin our staff presentation to give you an overview of the review process and what is in the staff report, followed by a health review by Dr. Ostro.

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DR. DRECHSLER: Good morning.

I'm Deborah Drechsler from the Air Research Division of the Air Resources Board. And my presentation this morning will give you an overview of the standard-setting process in California.

We'll go over the definition of an ambient air quality standard, the Children's Environmental Health Protection Act requirements, the regulatory process, the standard review timeline and the role of the Air Quality Advisory Committee, which we call AQAC.

Dr. Bart Ostro from the Office of Environmental

Health Hazard Assessment, commonly called OEHHA, will then present the basis and rationale for the recommended revision to the ambient air quality standard for ozone.

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DR. DRECHSLER: In California, an ambient air quality standard is the legal definition of clean air. It has 4 elements, including a definition of the pollutant, an averaging time, a concentration and a monitoring basis.

California ambient air quality standards are based solely on public health considerations. Although standards provide a basis for preventing or evading adverse health effects, they do not include consideration of such things as attainment designations, feasibility or cost of controls or of any specific control measures. The process for making air attainment designations is specified in sections of the California Code of Regulations that are unrelated to those we have opened in the present regulatory action and have no part in the regulatory action under consideration in this meeting.

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DR. DRECHSLER: California ambient air quality standards represent the highest pollutant concentration for a given averaging time that is unlikely to induce adverse effects in anyone who undergoes the defined exposure.

State law requires that ambient air quality standards incorporate a margin of safety to take into account potentially sensitive people who are not included in the available scientific studies.

Risk assessment, the number of people likely affected or the likelihood of any specific individual experiencing the exposure defined by the standard are not considerations.

The standards are staff's best estimate of the greatest exposure that will be without effect in anyone who undergoes the exposure defined by the standard.

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DR. DRECHSLER: The Children's Environmental Health Protection Act, which is also known as Senate Bill 25 authored by Senator Escutia and passed in 1999, required that ARB and OEHHA perform a preliminary review of all California ambient air quality standards to determine whether there was evidence that any might be inadequately protective of public health, with a particular emphasis on infants and children.

The Act also required that standards judged to be possibly inadequate be prioritized for full review. This process was completed in December 2000.

Recent initial review concluded that most of the California ambient air quality standards might not

adequately protect the health of the public including infants and children.

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DR. DRECHSLER: The standards founds possibly inadequate were then prioritized based on the extent of risk to public health. The standards for PM10 and sulfates were prioritized as being of the greatest concern, and full review of the PM10 and sulfate standards was completed in 2002 and revised standards became effective in 2003. Ozone was prioritized to be the second standard to undergo full review and the hearing today is part of the standard review process.

The nitrogen dioxide standard review has begun and we anticipate release of the staff report and recommendations later this year.

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DR. DRECHSLER: We're concerned about ozone because the health effects are significant and wide ranging. A large body of data, including hundreds of scientific papers, have consistently reported significant respiratory health effects. We are also concerned because ozone levels frequently exceed the current standard, meaning that many California residents are at risk of experiencing adverse health effects multiple times per year. There is also evidence that children may be

especially vulnerable.

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DR. DRECHSLER: The federal Clean Air Act gives California authority to set its own ambient air quality standards in consideration of statewide concerns. Because the California ambient air quality standards are State regulations, the federal laws pertaining to the processes and procedures for setting standards do not apply. Instead, we must follow the process of procedures outlined by the California Health and Safety Code and the California Administrative Procedure Act.

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DR. DRECHSLER: This slide, which is rather complex looking, but it outlines the process for promulgation of State regulations. The process starts with release of the draft staff report and recommendations. Many ARB and OEHHA staff and several contractors contributed to the staff report under consideration today.

OEHHA placed the central role of providing the recommendation for the standard based on the reviews contained in the various sections of the report. The report is released to the public for a comment period and is also forwarded to the Air Quality Advisory Committee for their review. And the report and recommendations are

peer reviewed by the Air Quality Advisory Committee at a public meeting. This review is mandated by the California Health and Safety Code.

I will tell you some more about the Committee on the next slide.

The public is invited to comment to AQAC on the draft report and recommendations and AQAC will consider those comments as part of the peer-review process.

Following receipt of AQAC's written comments on the report and recommendations, staff will revise the report as necessary to address those comments and those of the public. The revised report will be released for an official 45-day public comment period, after which the report and recommendations will be presented to the Board.

We will hold some public workshops during that 45-day comment period and will accept public comments on the revised report up to and including at the public hearing at which the Board will consider the item.

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DR. DRECHSLER: The California Health and Safety Code requires that the scientific basis of ambient air quality standards recommendations be peer reviewed. The Air Quality Advisory Committee fulfills this function. The members are appointed by the President of the University of California and each is an expert on one or

more of the subjects discussed in this staff report.

The Committee will be reviewing the report and recommendations in this meeting and will be providing staff a written report on their findings. They will also be considering the public comments that were submitted in writing and also the staff's responses to them.

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DR. DRECHSLER: This slide gives the timeline for ozone standard review. The draft report being considered this morning was released on June 21st, except for the health benefits quantification, which was released in August.

We held public workshops in Sacramento, Los Angeles, and Fresno during July and August. After AQAC's review, we will be revising the report and issuing it again for the 45-day comment period and will be holding additional workshops and accepting public comments up to and including at the Board hearing.

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DR. DRECHSLER: The report under consideration today contains chapters on the physics and chemistry of ozone formation and deposition; background ozone in California; ozone precursor sources and emissions; monitoring method; characterization of statewide ozone concentrations; welfare effects, including forests,

agriculture and materials; health effects and a quantification of health benefits estimated to accrue with attainment of the proposed ozone standards.

The report was written by a number of ARB and OEHHA staff and several contractors including Drs. Patrick Kinney, David Grantz, Charles Plopper, Ed Schelegle and Laurel Gershwin.

Tomorrow the Committee will be receiving oral comments from the public and will discuss the written comments and staff's responses to them.

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DR. DRECHSLER: To give you a context for today's discussion California currently has one ozone standard with an averaging time of one hour and a concentration of .09 parts per million. Ambient ozone concentrations are currently monitored by an ultraviolet absorption method.

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DR. DRECHSLER: The recommended revision to the standard, which OEHHA proposed and with which ARB concurs has several parts. We recommend retention of ozone as the pollutant definition; establishment of a new 8-hour average standard at .070 parts per million; and recommend retention of the current 1-hour standard at .09 parts per million.

We also recommend that the current ultraviolet

absorption monitoring method be retained and that all federally approved ultraviolet absorption samplers be adopted as California approved samplers.

This last recommendation will not result in any changes in current monitoring practices and will align California's monitoring methods with those at EPA.

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DR. DRECHSLER: I would now like to introduce Dr. Bart Ostro from OEHHA who will discuss the basis and rationale for the recommended revision to the State ozone standard.

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: Thank you, Deborah.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: I will speak loud. So if it's too loud, let me know. First I want to welcome the new members of the AQAC and say hello to the older members, the few older members -- or former members of AQAC, I should say.

(Laughter.)

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: And so I want to welcome you, and also thank you for agreeing to take on this role of reviewing the science leading up to our proposed standard for ozone.

I'm here to represent the Office of Environmental Health Hazard Assessment, which Dr. Drechsler indicated is responsible for reviewing the scientific basis for the standard and then proposing a recommendation for that standard.

So I wanted to introduce some of the co-authors that were involved in the review process and in the Recommendations Chapter. Melanie Marty is here. She is the Chief of the Air Toxicology and Epidemiology Section. Shelley Green is in the audience, part of the air pollution epidemiology unit. Pat Kinney played a role from Columbia university. Jon Levy is not here from the Harvard School of Public Health, but he played a role in reviewing the studies for the benefits assessment. He and Tran from the Air Resources Board worked a lot on the benefits section.

And also, because of budget cuts several years ago, we lost some of our staff and we're happy to have Deborah Drechsler play a major role in terms of reviewing the chamber studies for us. And we thank her for that. Sorry, if I've forgotten a few people, but -- Daryn Dodge who worked on the toxicology chapter. And is George here?

Yes, we have George Alexeeff, who is the Deputy Director for Scientific Affairs for our office. He's here today as well. So it's clearly a joint effort here.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION

SUPERVISOR OSTRO: As Deborah indicated, we have recommends to retain ozone as the pollutant definition. We've recommended establishing a new 8-hour standard of .070 -- notice the 3 decimal points there -- not to be exceeded. Retained the current 1-hour standard of .09 ppm not to be exceeded and to retain the UV monitoring system.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION

SUPERVISOR OSTRO: Now, as I indicated, two of you were here for the particle review that we did 2 years ago. And you may recall that in that case most of the evidence was based on the epidemiologic literature, with some support from animal toxicology and a little bit from human controlled studies.

Ozone, we have quite a different story. Here the primary basis for the standard is the control human studies with support from the animal tox and the epidemiology. We have literally hundreds, many, many hundreds of studies to draw on from all 3 of these levels of scientific inquires. We were quite fortunate with ozone to have a large wealth of information.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION

SUPERVISOR OSTRO: Now, since we do draw a lot of evidence from the human chamber studies, there are several issues related to those that we didn't talk about regarding particulate matter in our last go round.

Specifically, one of the endpoints that we looked at quite carefully are changes in lung function. And traditionally there has been questions about how relevant, how important are these changes in lung function. So questions like this we referred to the American Thoracic Society, criteria for adverse air pollution effects. A committee that's several times looked at this issue. It's a nationally recognized committee made up of experts in the field.

And their recommendations, which have been published, indicate that their concern about physiological and pathological changes that interfere with normal activity, they label adverse, episodic or incapacitating respiratory illness; permanent and progressive respiratory injury; reduction in quality of life; lung function changes with concurrent symptoms; and not surprisingly they label as adverse hospital admissions and mortality as well as populationwide effects.

So we draw on the ATS findings in this case.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION

SUPERVISOR OSTRO: Another important thing about ozone, which we didn't really deal with with particles is the evidence that from the controlled studies, the acute health response is related to inhaled dose or effective dose as it sometimes is called, which is the product of ozone concentration, ventilation rate and the exposure duration.

And concentration appears to play a very important role in the inhaled dose, acute health responses are proportional to concentrations of ozone. And that the control studies protocol attempts to Mimic exposures of those thought to be at the greatest risk. Specifically, children and adults who exercise or are outside for long periods of time or are working outdoors over long periods of time.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION

SUPERVISOR OSTRO: The initial studies on human exposure in controlled settings really began in, I think, the late sixties and mid-seventies and went on through the eighties focusing on 1- to 3-hour average exposures. And these studies showed a wide range of effects in the controlled setting that we summarized here; that there was lung function decrements in terms of FEV1 and other outcomes, noted at .12 ppm. One study below that at .10 did not

find an effect.

Increased respiratory symptoms were found at .12, but again not a .10, specifically cough was found at .12. And one study of children, which was not noted there, pain on deep inspiration and shortness of breath were found in children with a P-value of .009. So you might also want to consider that at .12. And then in an adults studies of other endpoints found effects at higher levels, pain on deep inspiration and shortness of breath were found at .24 ppm.

These 1- to 3-hour studies also showed increases in airway resistance at .18 and airway inflammation at .20.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION

SUPERVISOR OSTRO: Now, over time scientists realized that the duration of exposure played a very important role, and there was an attempt to look at longer exposure periods, 6.6 hours to 8 hours of exposure, and to determine what kind of responses were observed at those longer concentrations and at lower -- sorry, at lower concentrations of ozone and longer periods of exposure.

In all cases exercising people were used, usually a moderate level of exercise in this case. And for the shorter exposures for the 1- to 3-hour exposures sometimes

heavy exercise was used in order to increase the ventilation rate and the inhaled dose.

These protocols usually involved more moderate levels of exercise over longer periods of time. And these studies have shown now pretty consistently that lung function decrements occur at .08 ppm in terms of 6.6- to 8-hours exposures, increased respiratory symptoms also occurring at .08, as well as increases in airway reactivity and airway inflammation.

There have been a few studies below .08. Dr. Adams is one of the people who conducted one of the studies, .06 where no group level effect was found, but there were several individuals who were particularly responsive at .06. And another study showed basically no group level effect at .04 ppm.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: So what are the things that is important to observe in this graph -- and let me break out my laser pointer here -- is that when we're comparing clean air versus .08 and .12, that after about the 3rd or 4th hour of exposure, under these paradigms, increases in FEV1 became quite significant, ending up in this case with with about a 4 percent change. And the range on a group level has been about 2 to 7 percent change after the 6.6

to 8 hours of exposure. And again a dose dependent relationship as you go to higher levels.

But what is particularly interesting is that there are some strong responders within this group. Whereas, the group change might only be several percent. This study by Follinsbee showed that almost 30 percent of the subjects had an FEV1 change a 10 percent or more. And 10 percent of the subjects had a 30 percent or more change in FEV1. So quite a significant change among a subset of the subjects.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: And likewise with longer term exposures, in this case 6 hours -- 6.6 hours, total symptom scores increased depending upon what the concentration and duration. But at .08 after 4 hours of exposure, the symptom scores increased dramatically at a higher exposure, the increases at an earlier level. So clearly effects occurring with several hours of exposure at .08.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: Some additional considerations about the chamber studies that we wanted to mention, but we reviewed in our chapter.

The issue of attenuation. It's observed that after multiple days of exposure, there is some reduction in response in terms of FEV1 and symptoms. Usually after the second day of exposure, the response tends to diminish.

The studies have also found now, though that for some individuals there actually is no attenuation. And that it's possible -- these are usually after fixed doses over several days. It's possible that one study at least has shown that after several days at a fixed level followed by an increase in a higher dose, there was an increase in response in terms of FEV1. I think in symptoms as well. And that inflammation looks like it continues that there is no attenuation in terms of the inflammation over several days.

Also, a study by Henry Gong in '97 showed that he used a very high dose, I think .4 over 2 and a half hours or maybe 3 hours of exposure. Again he showed an attenuation. But after exposure stopped for 4 days or so, and then the .4 was repeated, everyone -- not everyone, but people in general tended to respond as in the first day or 2, so there was a 4 to 7 day recovery period followed by a full response after that.

Other factors to note are that we usually see the same people responding. There are studies that look at

individuals over multiple periods, and it does seem to be there there's a subset of people whose responses are replicatable.

And also when people have looked within this group of people being studied, when researchers have looked at that, again it's usually a cohort of young adult males, for the most part. And people have tried to look at factors which may predict who are the responders. It's very difficult to find factors that explain the response. So for the most part we don't know who these responders might be over and over.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: People have also looked at different demographics to examine whether factors may affect the degree of responsiveness. There's been only a few studies looking at different gender, age, S-E-X and race. And there is real insufficient data to draw much conclusion. But these issues are of concern for those economic justice issues. Basically the only thing that's been found is there's an age effect that older individuals seem to be less responsive.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: In terms of the animal tox studies,

they generally support the human studies. They demonstrate increased air resistance and inflammation at relatively low levels. They indicate that the injury repair cycles can cause fibrosis. And they indicate that there's changes in the airway architecture with chronic exposure to high concentrations, usually greater than .20 ppm.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION

SUPERVISOR OSTRO: Moving on to the epidemiologic studies. There's both advantages and disadvantages to the epidemiologic literature, which has increased vastly since the mid nineties, and there's now a lot more studies to draw on. When U.S. EPA did the review in '96 and '97 and we did our last review in '86 and '87, there was relatively few studies. There was a lot of questions about these studies and the software wasn't there.

But over the last roughly 8 to 10 years, there's been a wealth of new information using epidemiologic methods. Now, of course they examine real world exposure conditions, a wide range of possible exposures. They look at many different populations potentially vulnerable populations, as opposed to the human controlled studies.

So these studies can look at elderly people with preexisting heart and lung disease. They can look at

infants and children. They can look at asthmatics with all different degrees of severity. They can look at varied endpoints, including mortality and hospital emissions. They can look at longer periods of lags of several days or weeks. And also they can look at long-term exposures over several years.

So there's a lot of advantages to these studies. But as with everything there's always some disadvantages. So there is uncertainty about the relevant exposure average in a lot of these studies, since the 1-hour, 8-hour and 24-hour exposure in a given day are highly correlated. It's had to know exactly what the relevant and most important averaging time is in these studies.

It's unclear sometimes the time to response, whether it should be a 1-day lag, a 1-hour lag, a 3-day lag, whether you should use 3 days of cumulative averages and so on. And also the shape of the concentration response function. People have typically looked at either logistic function or linear functions, but a wide range of functions are available.

And basically they have not really been fully explored, unlike particles -- particulate matter, which has been of great interest to researchers over the last 15 or 20 years. There's been a lot of sensitivity analysis done. Ozone studies have not had the full set of

sensitivity analysis that particles have had. I suspect over the next couple of years there will be a greater focus on some of these issues.

Concerning sensitivity analysis, there is some concern about confounding and effect modification. There's questions about what the effects are of season, weather and co-pollutants, and issues of exposure assessment.

Very briefly, I should say that in general it looks at as -- the software available to look at these potential confounders as is software has come into play, you can look non-linear functions, and look really carefully at seasonality and time trends and so on. It seems that the ozone signal actually gets a little stronger as you control for time and weather more completely.

But it should be stated that the study results, the epidemiologic study results are certainly not consistent for just about every endpoint, we have both positive and negative findings, which may be not surprising given the relatively small relative risk that comes out of these studies. So less people are very careful in the modeling and it's very possible to get a null result.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: But what do these studies tell us as we reviewed in our document, we find respiratory hospital admissions for children under 2 and for all ages combined. We find emergency room visits particularly for asthma. There's studies that indicate school absences and respiratory symptoms among children, and respiratory symptoms among adults related to ozone exposure.

There's a study from Southern California now indicating that with exercise actually new onset of asthma seems to be occurring along with ozone exposure. There's some long-term studies that indicate that long-term exposures can be related to changes in lung function.

And finally, there's some studies that indicate that both short-term and possibly long-term exposure to ozone, particularly in the summertime, might be related to premature mortality.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: So what is our basis for our 1-hour standard, that we already have in effect and we're suggesting should be retained?

First of all, as we've indicated the chamber studies report effects of lung function and symptoms therefore meeting the ATS criteria at 0.12 ppm. And

there's a wide range of epidemiologic studies suggesting adverse effects below .12. Many of these studies go down almost to background levels of ozone. But again we're not sure exactly what the most relevant dose is or concentration is from these studies, but there's a lot of studies indicating adverse effects.

As we indicated in the document, there's a hint from the emergency room studies that there might be something approaching a threshold concentration level. There were some studies showing effects lower than they used, but it looks like somewhere in the range of .075 to .11. Somewhere in that range there begins to be a diminution of effects in terms emergency rooms visits. And we don't know if that's a real threshold or just that the signal gets very weak at those lower levels.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: The other basis includes concern for inflammation. So this standard provides additional protection for that. We want to protect against effects of peak exposures. The chamber studies, for example, show that when you -- instead of looking at square wave that is constant concentrations of exposure, if you have a triangular exposure, that there is short-term peaks, those 1-hour, 2-hour peaks still play an important role in terms

of eliciting lung function changes.

So we want to protect against peaks, particularly for certain subgroups. If these epidemiologic studies are true, then there's certain subgroups that clearly are not covered in the chamber studies, including infants and elderly people with preexisting disease. So we wanted to add a safety margin to protect these other potential susceptible groups.

And finally, we thought the studies indicated that we should protect against peaks in areas that may be a federal 8-hour standard or California 8-hour standard of .08 or .07, but still have relatively high 1-hour concentrations.

Now, as the whole average -- long-term average of ozone drops, we being to see less and less 1-hour peaks. But as we indicated in our chapter and there are still areas that, under a .08 8-hour standard would see some relatively high 1-hour concentrations, which we thought people should be protected against. So that's our basis for the 1-hour -- of retaining our 1-hour standard.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: Our 8-hour standard, again we first focused -- most importantly focused on the chamber studies, which report symptoms, lung function changes,

airway responsiveness at -- and inflammation as well at .08 ppm. Again, some individuals exhibited large changes at .08 over 6.6 hour exposure.

The epidemiologic studies again suggest adverse effects at concentrations likely below .08 ppm.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: Again, drawing on the emergency room visit studies suggested a lower effect threshold, somewhere in the .065 to .09 range. We don't know exactly where that is. Adding a safety margin again for highly responsive individuals, including children and other susceptible groups.

We added the concern that we wanted to provide protection in areas with low long peaks, which a lot of the inland California experiences. They don't experience the 1-hour spikes, rather they have spikes of 3 or 4 hours. So in areas that could meet a 1-hour standard of .09 which still might be high levels of longer term exposure that we thought needed protection.

And finally once you draw the whole average -- the whole distribution of ozone down, it also means that we would have protection against long term, in this case really long term, several years or more of exposure against some of the potential effects that have been

observed.

So that's our basis for the 8-hour exposure.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: Now, SB 25, which required the review of these standards, also asked us to focus on infants and children particularly, so we had a couple of findings in our report to meet that mandate. And specifically we found no evidence from the chamber studies that children respond to acute exposures at concentrations lower than where we see responses from adults.

That exposure patterns might be of concern. That there's frequent high exposure due to outdoor activity. And that there's a greater exposure per unit lung surface than for adults.

There's also some concern about susceptibility. There's studies that indicate that early exposures may affect lung development, may reduce long-term lung function. There was a study that just came out in the past year that showed that children in Los Angeles had -- it looks like -- permanent lungs function changes. They were observed at age 18. And there's studies now that indicate induction of asthma might occur from early exposure.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: We didn't find much evidence for interactions among pollutants, something else that SB 25 asked us to look at.

And we do find several health outcomes that are specific to infants and children, including things like school loss, hospital admissions, decreased lung function and possible onset of asthma.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: Now, one of the things that we conducted, which was not part of our -- didn't factor into our recommendation into our consideration of a standard, but was presented for public information purposes, was the question of what are the health benefits that might be expected from attaining our proposed standards?

So we used a methodology similar to that used by U.S. EPA in their reports to Congress under Section 812 under several regulatory impact analyses that EPA has conducted, as well as some other published papers that have come out. And we see very significant effects in terms of relatively minor occurrences like restricted activity days and school absences, and quite severe effects, such as premature mortality.

But again, these conclusions -- these findings

didn't go into our consideration of an actual standard. It's more the implications of what that standard will be.

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OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: So the final slide here summarizes our recommendations again to retain ozone as our pollutant indicator, to establish a new 8-hour standard of .070, not to be exceeded, to retain a current 1-hour standard of .09 that we currently have in place, and to retain the UV monitoring method.

So this ends my overview of the health basis for our recommendations and the benefit assessment.

CHAIRPERSON KLEINMAN: Thank you very much, Bart. Just a point of clarification as long as you're standing there. The retention of ozone as the indicator standard, do you want to elaborate on indicator standard for us?

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: Well, it was other potential oxidants that could be in there.

CHAIRPERSON KLEINMAN: So this is like taking into account things like peroxides in the air for which there is virtually no health data to base it on; or nitrous oxide -- nitrous acid rather, but excludes NO2 as the other primary oxidant gas. So really we're looking at ozone as the indicator for all oxidant gases other than

NO2, is that correct?

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: I think that's probably correct, sir. This goes back to -- this is a throw-back to the old days where we actually had an oxidant standard, and we were moving from a pure oxidant standard to an ozone standard, so we just wanted to make sure that that was clear that we're still moving in that direction and keeping that direction, yeah.

CHAIRPERSON KLEINMAN: But, I guess, the distinction is we used to use a chemical method for analyzing, which actually responded to these other oxidant gases. Whereas, the ultraviolet method, as far as I know, doesn't really respond to at least some of these. So I was just wondering whether we need to continue that terminology that ozone is the indicator for oxidant gases.

Really, the way we're monitoring now, unless perhaps the monitoring group wants to comment, ozone is really an indicator for ozone.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: Dr. Kleinman, if I can kind of elaborate on that. Kind of what Dr. Ostro mentioned was correct that back -- actually when the first oxidant standards were set were back in 1959. And you're right, originally then they were done as an oxidant standard included many compounds. And it

wasn't until, I think, about the 1970s we actually changed it to oxidant is measured as ozone, and then changed it to an ozone standard. So it's a little bit of an anachronism left over from the old days.

But it is true that as part of a standard you have to name the pollutant that you're considering too. So probably it's not so much that ozone was the indicator of oxidant nor is ozone the pollutant of concern.

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: So maybe we should change that terminology then.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: Yeah, I'll make a note of that and make that change.

CHAIRPERSON KLEINMAN: Okay. Does anybody have specific questions for Dr. Ostro or Drechsler before we move on to the specific comments on the chapters?

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: I would note that right now the agenda said we're taking a break, but I don't think we have refreshments yet, so unless the Committee needs to, I think we ought to just keep on going.

CHAIRPERSON KLEINMAN: If there's no objections to that, I think that's a good idea. We are a little bit over time.

So, Richard, do you have any other comments that

you want to make at this point?

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: I don't, Dr. Kleinman. I think I'm just going to leave it up to you as the chairman to now take the Committee's comments.

CHAIRPERSON KLEINMAN: Okay.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: And I make one point, too, is we do have staff available to answer questions you may have. Part of this is you're hearing the comment itself. If you have questions, we have staff available as well.

CHAIRPERSON KLEINMAN: Then I think as per the agenda -- let me just make sure I'm reading it right -- that we'll start off with discussion of the exposure, background and monitoring chapters of the document. And I'd like to ask Peter Green to discuss some of those aspects, and then we'll go around the table.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: Dr. Kleinman, if I could interrupt for one second, did you have a presentation you wanted to make at this point or was it later on?

CHAIRPERSON KLEINMAN: Well, actually that's a good point. I did get ahead of myself, but, yes, I did have a couple of slides just to put a framework down.

(Thereupon an overhead presentation was

Presented as follows.)

CHAIRPERSON KLEINMAN: So in preparation for this, the Committee received copies of the draft document, the comments and responses to the comments in late November. And I asked each of the Committee members via an Email to look at the document and specifically at the chapters relevant to their areas of expertise to answer some questions.

And the basic questions were related to were the key studies or relevant studies properly identified and properly interpreted? Were there omissions to the body of literature that might alter the conclusions in any substantial way? And were things either over or under interpreted?

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CHAIRPERSON KLEINMAN: With respect to susceptible populations, have any specific populations been missed? Or should there be other groups taken into account?

Also, about 5 or 6 years ago, we had an extensive review pollutant by pollutant to determine whether the existing standards were adequately protective of infants and children, ozone being one of those pollutants. And in fact those were the -- those discussions were the basis for setting the priorities for reviewing the health

standards in sort of a chronological sequence with PM being the first to be reviewed an ozone now being the second of the priority pollutants.

And one of the issues were, at that time as of 5 years ago, were there you know -- what would be adequately protective. And for ozone there were some reservations which were taken into account. But since then there have been several studies written on infants and children, and so we charged the Committee was to review whether those issues were specifically updated properly.

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CHAIRPERSON KLEINMAN: Are there other issues that need to be considered, additional literature that has not been represented? And were things like multiple pollutant effects taken into account?

These are very difficult problems to deal with, multiple pollutants are certainly not the way we're dealing with setting regulations. We are currently setting regulations on a point-by-point basis.

But when we review the PM standard, the Advisory Committee strongly recommended that as we move to the future, we do need to start recognizing that pollutants are presented to the people as an ensemble, where we're being bombarded by PM and ozone and other things at the same time.

And sometimes there are interactive effects. And I think for a great you know -- to many issues they may indicate why we have some inconsistencies in some of the findings that we have out there when we try to look at only one topic at a time.

So as we move through the process, eventually we should start thinking in terms of more than one pollutant. It's a difficult issue, especially from the standard-setting process. But they're all interactive. For example, to control ozone, we really have to control precursors. We're not really controlling ozone per se. We're controlling NOx. We're controlling hydrocarbons, a number of other things that relate to the creation of ozone in the atmosphere, because it's a secondary pollutant.

And so these things have interactive effects not only on health, but on the way that ozone is formed and removed from the atmosphere.

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CHAIRPERSON KLEINMAN: There are always uncertainties in doing these evaluations. And it's impossible to do a study like this without taking uncertainties into account. The Committee was asked to make sure that, you know, the important uncertainty issues were at least addressed in the presentation, and to

determine whether uncertainties were adequately treated.

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CHAIRPERSON KLEINMAN: Are there differences in exposure patterns? Ozone is a pollutant that has dyonic patterns. It has seasonal patterns. There are differences in indoor and outdoor exposures. And there are differences in the way individuals that are exposed to the ozone. And so it is important that in looking at the relevant studies, that the exposure patterns and differences were taken into account.

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CHAIRPERSON KLEINMAN: And finally, when it comes to setting the standard, is it -- I use the word transparent, which might not be exactly the way to go, because what may be transparent to Dr. Ostro or an epidemiologist and someone who does a fair amount of modeling might be rather opaque to me. But, you know, has an adequate case been made and has the data been openly presented, and are the standards supported by some kind of rational.

So if you use ozone as an indicator for oxidant pollutants or for ozone, perhaps we can modernize our terminology, is the 1-hour standard and the 8-hour standard as described appropriate? And is the form of the standard -- would you state it to be or not to be exceeded

quantity accurately described so people can understand what that actually means in terms of this.

So that sort of framework that the Committee started with in looking at this very formidable document to try to make sense out of those questions, as well as, you know, all the other issues raised by the standard setting process. So, at this, point I'm going to go back to my seat. We will talk about future research as well.

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CHAIRPERSON KLEINMAN: And there might be other research issues, but we don't have to deal with those at this point.

So having said that, I'd -- yes.

ADVISORY COMMITTEE MEMBER DELFINO: Yeah, I agree it's important to look at the terminology indicator gas, but I'm not sure -- Bart, I'm not sure if it's wise to necessarily drop that terminology. And the reason I say that is that from my perspective as an epidemiologist, I look at ozone as an indicator gas in my studies.

I mean, I don't assume that the effects of ozone are just simple due to ozone. So, yeah, I know the monitoring technology, that's what measures UV is ozone nothing else. But I don't know about -- I mean, I think the terminology indicator gas is actually quite a good one, because what you're seeking to control is ambient

ozone. And you're not controlling anything else that goes with it.

So if we're going to use the epidemiology data in particular as a basis for those standards, you have to retain that terminology. If you're going to solely rely on the chamber studies and the animal toxicology studies, that's a different story.

ADVISORY COMMITTEE MEMBER HAMMOND: I think a lot of what you say make sense in that epidemiologist clearly included in these other oxidant gases the chamber studies are of ozone itself. I think the question would be if we're monitoring ozone itself, one would have to demonstrate that that was a good surrogate for all oxidant gases.

And if in fact it's not, unless you could share that it was, I think you're misleading to say that a measurement of ozone is an indicator for all the oxidant gases. And so I think you're safer saying you're monitoring for ozone, you're regulating for ozone, protecting ozone, however these other oxidant gases, which are then implicated by the epidemiologic studies haven't been controlled necessarily.

ADVISORY COMMITTEE MEMBER DELFINO: And that brings me to the next point that I left out, that I think part of our discussions should also look at that

literature and look at evidence that ozone is a good indicator of gas for other pollutants, even some that we haven't thought about or were not discussed in this document, like photochemically generated ultrafine particles.

In other words, but -- and perhaps you could lead that discussion, what is the -- or somebody who knows about this, could begin to look at this. What is the literature on the correlation between ozone and peroxides and other -- I think the Southern California Particle Center has done quite a bit of work in recent years on that.

ADVISORY COMMITTEE MEMBER HAMMOND: I think this is a very important question, but I also feel that's not what's been addressed in these documents that we have. That would require a lot. And I think that there may be a question whether in the sense of -- and I'm not sure what the format is here -- but to protect the health of Californians, the answer may be that having only an ozone standard would insufficiently protect that that might be the interpretation.

But I think we have inadequate data here. The data we have here relate principally to ozone, but we might want to put on the agenda the question of other oxidant gases or other what ultrafine particles are

generated as a result of some of these oxidant gases. I think they're very important points in terms of health.

But I guess from for me -- and actually I was wondering about that earlier. I have -- as far as I could see, this really was ambient air quality standard for ozone. And so I felt comfortable with ozone being measured, where it only measures that.

I do believe the other oxidant gases are important for health effects. But we wouldn't be measuring them by the methods that are given. And I'd start being very insecure. I don't think the documentation here is sufficient to do that.

ADVISORY COMMITTEE MEMBER DELFINO: I mean, it's clearly an impracticality to do that, given the work of the monitors as they are.

ADVISORY COMMITTEE MEMBER HAMMOND: So I think -- I mean, I would like to acknowledge that your point is really important for health, at the same time as saying, at least from my point of view, and all I can speak is we've got data for work for the ozone, in terms of the documentation that's here.

But I do agree that the epidemiology actually is included in these other issues and they really should not be neglected.

ADVISORY COMMITTEE MEMBER DELFINO: Okay.

CHAIRPERSON KLEINMAN: And it may be that what we want to do is make a recommendation for future research to elucidate the degree to which ozone can be a surrogate for some of these other gases. Certainly, there is a very strong correlation between peroxides and the ozone levels in the air.

There may be a poor correlation with other things, because they're more rapidly removed. And I think we have to play the hand we're dealt. And what we're measuring now using the ultraviolet absorption at a specific set of wave lengths is primarily ozone. And I don't know that we have enough information to say that other things are being measured in addition to that.

Anyway, I'd like to allow Peter to take the floor.

ADVISORY COMMITTEE MEMBER GREEN: Thank you. In terms of reading through all the chapters, and to those closer to my background in chemistry, such as the monitoring and exposure dosimetry measurements and the extensive discussion of the background ozone concentration, I felt quite satisfied that overall the key issues were addressed, and that the literature had been adequately scoured and distilled.

And I think there may be public comment on background tomorrow and more discussion on it. I think

it's been well addressed in the written comments and responses.

And my primary, sort of overall, recommendation on reading through all the material was, again maybe just from my personal experience, a need to be careful with significant figures and the units in which things are reported. It's in some ways a trivial point, but it's also crucial that numbers not be truncated when they're not supposed to be.

And, in fact, there were -- I found one example of a federal EPA protocol that allowed truncating numbers and was effectively saying that 84 was less than or equal to 8, which was mathematical impressive, but following the letter of their procedure for an ozone concentration and doing so to meet the standard in the way they intended it to be met.

We're setting a different procedure here. And it needs to be abundantly clear where the significant figures are and what's the best unit to express them. And that needs to then be carried throughout reviews and documents and reporting of monitoring data and so on and so on. It could amount to a significant difference in whether future attainments are considered met or not met, and that's something that can be revised over the next short cycle.

That certainly in terms of the long-term

research, I see it's very interesting in many areas, including those already mentioned. And particularly in terms of background, the questions of what background ozone can occur at different seasons, and particularly different elevations.

Most of California is at low elevation, but the population of California is at low elevation and the known air pollution problems are a certain season of the year. And so I think it's abundantly clear what's being tackled here. But in the future research I could see that continuing to be important, and being refined in studies and overall understanding of atmospheric chemistry in general.

CHAIRPERSON KLEINMAN: Thank you very much.

Did anyone else have specific comments?

Kathy.

ADVISORY COMMITTEE MEMBER HAMMOND: I would like to commend the staff for an excellent document. I think -- I'm speaking specifically about the exposure chapters.

I think that this is a very complex issue. And I think that they've tackled this with a great deal of thoroughness, and I'm very impressed with that.

And I think again the background issue obviously is going to be coming up again I'm sure tomorrow. And I'm

not quite sure, because I'm new to this committee how to discuss these issues.

I had a couple of questions about some others. I don't know if we ask questions at this point?

CHAIRPERSON KLEINMAN: Yes.

ADVISORY COMMITTEE MEMBER HAMMOND: This is kind of like minor, but it was a big point in some comments. The stratospheric ozone intrusion. This is not an area that I do know. But my question is when those things happen, is that pretty apparent? It looks to me, from what I could tell, that one basically knows that that's what's happening, is that correct? That, you know, it's happening under certain weather conditions. It tends to really happen at higher elevations, from everything I was reading.

This is not like some sort of subtlety that just unbeknownst to anybody there's this intrusion. Is that a correct interpretation?

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: Let me get some of our staff up here.

ADVISORY COMMITTEE MEMBER HAMMOND: And you mean like right now or later?

CHAIRPERSON KLEINMAN: Now.

DR. Van CUREN: I'm Dr. Tony Van Curen, Air Resources Board Research Division. I had really hoped to

sit in the back and sleep today.

(Laughter.)

DR. Van CUREN: Regarding stratospheric ozone, it's a very dynamic situation, but the evidence that we have based on ongoing research, and there's a lot more to be done and we can thank to a large extent the interested global scale climate change and atmospheric pollution for a lot of recent and better understanding and better measurements of what's going on.

But the intrusion of stratospheric ozone down to the surface is driven by processes that require very strong mixing dynamics, that is in the latitude of California. Now, in the tropics and in the polar regions, the dynamics are different. But in the mid-latitudes the dominant vehicle by which stratospheric ozone is delivered to the surface in high concentrations is what's called -- what's sometimes called the tropopause folding event. It's basically a very strong turbulent structure associated with storms and fronts in the troposphere will incorporate a blob of air from the lower stratosphere and push it down to the surface.

And, in fact, there was once such event back in the 1970s that was documented in California, at least has been discussed in a number of contexts. But this is a relatively repair even. Recent studies to look at this

dynamic as an upper air phenomenon using ozone light or other things to allow you to look at the entire vertical structure, the atmosphere shows that these events are relatively common at altitudes well above any place that humans -- we're talking, you know, 5, 6, 8 kilometers and up. And unless you are in the Himalayas, that's generally not a big concern.

That it is a fairly common phenomenon, but that the frequency of occurrence decreases as you go to lower altitudes simply because the scale of turbulence it takes to push stuff that much farther down requires -- you know, you just have a natural distribution of the frequency of occurrence based on the frequency of the energetic structure of the these fronts.

ADVISORY COMMITTEE MEMBER HAMMOND: So would it be a reasonable assumption -- it seems to me that if that were to occur that could be identifiable as what's called an exceptional event?

DR. Van CUREN: Yes, it is. And in the case of 1972, stands -- I think it was 1972 -- stands out because there was an exceptional event determination made for that event.

ADVISORY COMMITTEE MEMBER HAMMOND: So one could acknowledge that these things happen. But when they happen, they're likely to be identifiably, they can be

called an exceptional event, and then not really be a major problem in terms of understanding when there's exceedances. It would not be an exceedance then, because it would be an exceptional event?

DR. Van CUREN: Right. That's the position that we take, is that we can recognize these and deal with them and that they're sufficiently infrequent, but we don't see them posing a significant barrier to our properly monitoring and recognizing the effects of anthropogenic pollution.

ADVISORY COMMITTEE MEMBER HAMMOND: I felt that I could infer that from the document, but I think it might be -- I don't know if this gets revised or where we go. But I think that's one of the things that could be made very strongly. You could actually just say that, that these are identifiable and can be dealt with and -- so that was -- as I said, I thought that was actually in there.

The only other kind of minor comment that I had -- this is just -- I have difficulty with acronyms. And I'd really like to have acronyms spelled out the first time they're used, you know, any place. And particularly sometimes the comments come in, as -- if the comments get folded in and those comments came in with acronyms in terms of spelling, just make sure that that's done.

But actually, I really think it's a wonderful document. It's a very thorough job. And I want to commend you on the effort.

CHAIRPERSON KLEINMAN: Just as a reference, the goal of our comments today and tomorrow will be to compare a written presentation to be presented to the staff. And based on those recommendations, they will write a revised report.

So our comments and things that we feel that have not been adequately explained goes to this issue of transparency that I mentioned earlier. If, to us, we weigh the document as written and explained, you know, whether deriving something from it or exactly how they're going to use it, for example, it's adequate -- it's not adequate necessarily to just say we will recognize something as an exceedance, based on some sort of tropospheric inversion.

If possible, it would be very useful to include some things specific, something concrete. I believe it was actually in the responses to some of the comments about acronyms, for example, looking at relationships between CO and CO2 and logical factors and things like that, as being the way you will identify an unusual occurrence, and then take that into account in terms of whether or not they're doing it as an exceedance on a

particular day.

Is that clear?

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: Dr. Kleinman, tomorrow when we go into our discussion of comments and responses, we'll go into mere detailed discussion of how to look at some of these stratospheric events and what type of analyses you might want to do with those. We can highlight those.

But some of these got into our comments, but some of them the work was done after the comments were developed and written comments were developed. So we'll try and to do that tomorrow when we incorporate those into them.

CHAIRPERSON KLEINMAN: Thank you.

Any other comments on those issues?

If not, in some of the comments that were I believe to be from the Committee members. Dr. Fanucchi, specifically had some comments about how adequately the dosimetry and -- not the dosimetry per se, but the exposure assessment for children and infants were presented.

ADVISORY COMMITTEE MEMBER FANUCCHI: Actually, yeah. The information may be in this document, but I found it very difficult to pull out the kind of information that I was looking for. Since infants and

children are such a large important emphasis on this review, what would have been nice to see is a comparison of the ventilatory rates, the total lung -- all the pulmonary functions that we know about children versus adults.

And so that we could maybe take some of the adult human data that we have and extrapolate it down to an infant or a child that would be playing outside. I think that would make the case a lot stronger for protection. I know that you mentioned that there's no evidence that children respond to lower doses of ozone than adults do. You don't really prove that case, without knowing how the dosimetry is between children and adults. It's sort of left unclear to me. So I think that would be very, very helpful to have a nice comparison between children and adults in there.

CHAIRPERSON KLEINMAN: Thank you.

Dr. Platzker, do you have any comments?

ADVISORY COMMITTEE MEMBER PLATZKER: Specifically on the dosimetry?

CHAIRPERSON KLEINMAN: Yes, on the sensitivity per se.

ADVISORY COMMITTEE MEMBER PLATZKER: Well, my focus is really on children who suffered an insult early in life. And my feeling is that this document can really

both excludes a very important population and that is the fetus. As most of you who follow this area know that environmental tobacco smoke amongst the fetus is more highly affected by it than are infants and children.

In fact, if you look again at environmental tobacco smoke, the impact on fetal lung development, fetal lung size at birth is more significant than what will happen in post-natal life with environmental tobacco smoke from mother or father or both.

So my concern is that we don't really know whether these studies are showing impact of long-term ozone exposure on the lung function of 10 to 18 year olds is really adequately referenced against what the impact is in a baby who's born to a mother who has been in a very high polluted area for ozone during her entire pregnancy.

Second, infants who have experienced neonatal illness, and I'll just reflect on 2. One is an infant who's born with a membrane disease, respiratory distress syndrome, born prematurely. We've measured their lung function following this insult, especially on those that have subclinical injury to their lungs, and found that the airway's resistance, which was a measurement that we no longer need to do because we have other methods is about 5-fold that of the healthy baby of the same age.

These children may not with just routine lung

function studies evidence impact of environmental pollutants, because, of course, their baselines or respiratory dysfunction is so significant that you may have to look in other ways, such as rehospitalization of acute exacerbations rather than just lung function to see this effect.

There are very few studies, or I could not find any, on the impact of ozone on the developing fetus. As you know, there's a recent study looking at carbon monoxide and PM2.5 on birth weight of infants, but this wasn't read for instance against ozone.

CHAIRPERSON KLEINMAN: So there is a need for additional research in those areas, and we should make that recommendation then.

ADVISORY COMMITTEE MEMBER DELFINO: Mike, the National Children's Study, the RFP was just announced, that's one of the things that they'll be looking at, really from before pregnancy through pregnancy and at the point of birth looking at environmental impacts on a whole host of outcomes. It's a huge cohort study. It's just starting.

ADVISORY COMMITTEE MEMBER FANUCCHI: Actually, there's a small subset of the research there showing that there are morphological alterations in the cerebellum of rats that have been exposed prenatally to ozone. And if

ozone's capable of altering cerebellum development, it wouldn't be surprising if it were capable altering lung development. So definitely I think we should make a recommendation that that be an area of research.

ADVISORY COMMITTEE MEMBER PLATZKER: The difficulty with that is that we now can measure lung function in a very sensitive manner after birth. It requires sedation, but the number of institutions that are able to perform those studies is really very few. But these would be very valuable studies, similar to other ones did, looking at the effects of environmental tobacco smoke on the development of the lung.

CHAIRPERSON KLEINMAN: Thank you. Another issue going back if -- is there anything else related to the exposure or background areas of the document?

If not, one of the other issues that was briefly discussed was, you know, related to the number of significant figures in the way the standard is expressed. And that's really a function of the precision of measurement with which we're measuring ozone. And precision measurement for a 1-hour standard is going to be somewhat different than our ability to precisely measure and 8-hour average. Because in the 8-hour average you've got many more data points that get averaged in.

And I was hoping that we could get a little bit

more discussion into the chapter on monitoring as to specifically we know that the monitoring method is ultraviolet absorption, but how many measurements are taken per hour, what is the averaging time of the instrument that goes into that. And does that support our not-to-be-exceeded framework?

I think it's important that that be explicitly stated in the document, in the chapter on that. As Dr. Green mentioned the number of significant figures is essential in deciding what the truncation or round-off is going to be. I feel that's an area that we really do need to address more explicitly. I'm wondering if the staff has any comment on that.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: Dr. Kleinman, would you like to handle the discussion of the monitoring method itself and our monitoring network or the instrumentation?

CHAIRPERSON KLEINMAN: Yes.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: We've got Ken Stroud from the Monitoring and Laboratory Division.

CHAIRPERSON KLEINMAN: Let's see.

Was this going to come up in a later discussion or --

AIR QUALITY SURVEILLANCE BRANCH CHIEF STROUD:

Not unless you asked us.

CHAIRPERSON KLEINMAN: Okay.

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: Let me just respond to the health side first before we do something on the monitoring. As I mentioned in the overview, we did recommend a 3 digit .070 as opposed to a 2 digit existing 12 hour. And the reason for that was the earlier standard of .12 was -- of .09 was based on, as I've indicated, the chamber studies at .12 plus a margin of a safety.

When we're talking about the 8-hour exposures, I indicated that we've seen effects at .08. Now, if we left a standard of .07, that would allow .0749 to be rounded down to .07, and therefore be considered acceptable.

We felt that a constant exposure -- periodic exposures of .075 roughly would not provide an acceptable margin of safety. Therefore, based purely on the health information, we felt we wanted to ensure an adequate margin of safety by actually dropping down to .070 and precluding the rounding off and acceptance of a level of .075. So that was the health based rational there.

ADVISORY COMMITTEE MEMBER HAMMOND: Just as a point of clarification, .070 has 2 significant figures, okay. .07 has one significant figure. And if you want to do it in ppb it would be 70. That gives you 2 significant

figures. So you could work it out how you want, but be clear on that, please.

CHAIRPERSON KLEINMAN: I think the key thing is, does the monitoring method really support that level of precision that when we state that .070 is not to be exceeded that we're not going to be allowing .0745 to be, you know, the representative. So it would be very useful to have this discussion, I think.

AIR QUALITY SURVEILLANCE BRANCH CHIEF STROUD: Okay. I'm Ken Stroud. I'm with the Air Resources Board, Monitoring and Laboratory Division. I'm the Chief of the Air Quality Surveillance Branch.

And I think there was 2 questions. One was question frequency of measurements. And these -- the UV photometry is a continuous method. So it's taking Measurements -- 2 to 3 measurements a second.

So when we talk about air or random air is averaged out, because the data are collected on an hourly average. So on each hour we average, you have thousands of individual measurements.

Also let me just state that when we calibrate the units, we calibrate to the nearest part per billion. We measure to the nearest part per billion and we report our data to the nearest part per billion.

And to assess the accuracy or bias of our

instruments, we conduct audits, annual audits of all the State and district ozone analyzers. And per EPA guidelines, we audit them at different levels, a high concentration, a middle concentration and a low concentration.

Since we're talking about .07 parts per million today, we looked at our average bias at the low concentration audits, and I have a transparency, but I don't see an overhead projector. So I'll just have to --

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: You want us to put that up?

AIR QUALITY SURVEILLANCE BRANCH CHIEF STROUD: While they're putting that together, let me just clarify how our audits worked on. Our audits are conducted by an independent group at the Air Resources Board. That's different staff from the monitoring staff, different management, different instruments, different transfer standards. So it is a performance audit in that they -- the gas is introduced through the probe just as ambient air would come through the probe.

ADVISORY COMMITTEE MEMBER DELFINO: When the 1-hour ozone concentrations for various reasons were reported, it's reported by 10 ppb's? In other words, it's rounded to .0 whatever? So in particular 10 ppb's or 1 PPB.

AIR QUALITY SURVEILLANCE BRANCH CHIEF STROUD: In that database it's to the part per billion?

ADVISORY COMMITTEE MEMBER DELFINO: In the database, but I mean when you say downtown LA and the average ozone concentration, is it in ppb's or?

AIR QUALITY SURVEILLANCE BRANCH CHIEF STROUD: Well, it depends. When we report the our data to U.S. EPA, we report it in part per billion.

ADVISORY COMMITTEE MEMBER DELFINO: Okay, but the standard is on .08 PPB?

AIR QUALITY SURVEILLANCE BRANCH CHIEF STROUD: Yes, right. And there's a conversion, when -- I mean, the designations are made where they are converted.

ADVISORY COMMITTEE MEMBER DELFINO: I mean, if -- this has always been confusing to me, you know, if the health effects occur at 80 ppb's, why do you then allow a districts to round down to 80 ppb's when they're really 84 and a half ppb's.

AIR QUALITY SURVEILLANCE BRANCH CHIEF STROUD: I believe that's set out in the standard.

ADVISORY COMMITTEE MEMBER DELFINO: That's federal procedure, okay.

AIR QUALITY SURVEILLANCE BRANCH CHIEF STROUD: Well, are we going to give up on that?

CHAIRPERSON KLEINMAN: I think we'll give up on

it.

AIR QUALITY SURVEILLANCE BRANCH CHIEF STROUD: Okay, maybe you can hand me back my transparency. I'll just read it.

CHAIRPERSON KLEINMAN: I think we can dispense with the projector. That shortens it up, so you can give him the transparency, so he can tell us what we would have seen.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: Just read out what you've got.

AIR QUALITY SURVEILLANCE BRANCH CHIEF STROUD: I apologize. Sometimes low-tech just doesn't fly.

CHAIRPERSON KLEINMAN: Go ahead.

AIR QUALITY SURVEILLANCE BRANCH CHIEF STROUD: What we looked at, as I said, we looked at our bias for the last 6 years. And since I'm reading this, I'll just look at the last year, 2004. Number of monitors audited is 132. And our average percent difference at this lower concentration is approximately .03 ppm to .08 ppm. The average percent difference is minus 1.26 percent. The standard deviation is 4.25. And we convert that to 95 percent confidence level and you get an upper level of 6.96 percent, lower level of minus 9.68 percent. And when we take those percentages and apply it to .070, what we're getting is plus 5 parts per billion, minus 7.

So what that means is, and I have a graph, so you can't see it. But if our analyzer is reading .070, and our actual concentration, a true concentration, could fall within the range of .063 part per million and .0775 part per million. So there is uncertainty in the measurement.

And I'll just turn it back to questions.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: And how this relates to us when Dr. Ostro bought it up, is that the standard recommendation was based on a health consideration basis. It's been in the designation process. I think Dr. Drechsler brought it up. It is a separate regulatory process. So we identify, basically a procedure as to how you identify attainment and nonattainment. And that's really rounding conventions and truncation events for identifying attainment and nonattainment that were created in the study.

So we have 2 different processes. And that's why I think when we all look at the document -- the scientific literature and saw effects of .08, and our concern was again knowing the truncation felt that .0749 was more than .05 would be.

CHAIRPERSON KLEINMAN: Thank you very much.

AIR QUALITY SURVEILLANCE BRANCH CHIEF STROUD: So we're making copies.

CHAIRPERSON KLEINMAN: That would be very

helpful.

I think it would be very useful to have a brief discussion of that during the chapter, and also to make it very explicit when you say that the standard is not to be exceeded. You know, we're not to exceed the standard 7. And then that implies a certain degree of precision in the measurements. I think that needs to be explicitly stated somewhere, so that when they do set the appropriate control strategies, they will have that embedded in the process.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: We'll do that. I might point out that I think what happens too is we wrote the initial monitoring and exposure chapters way before we actually had finished the health review.

So I think some of these issues didn't get the data used in the chapters. I think also we wanted to actually keep the designations from standard setting, because we always speak out about having 2 separate processes. But I think kind of what I've heard and is probably right is what we've been -- is a little confusing, because a little bit of information is good but maybe it's not enough. We need to express that.

ADVISORY COMMITTEE MEMBER HAMMOND: Do I hear correctly that you really want to be absolutely sure that

no one goes above .070? That's your goal?

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: (Bart Ostro nods head.)

ADVISORY COMMITTEE MEMBER HAMMOND: I think that that's the your goal from the health point of view. What I hear Ken saying is that -- saying if setting a standard of .070 where the monitoring equipment will be at, will not guarantee that.

I think that -- my guess is that Ken would say that you would need to be setting it at .060 to ensure that people would not be exposed to anymore than .070. Is that correct?

AIR QUALITY SURVEILLANCE BRANCH CHIEF STROUD: Yes.

ADVISORY COMMITTEE MEMBER HAMMOND: I think you need to think about that. If that's really what your goal is, that's not what you're achieving given just the real life of what the equipment does.

CHAIRPERSON KLEINMAN: But on the other hand, it is consistent with the health data that you use in establishing the health basis for the standard, because we're all using the same information that you need. So to some extent that is taken into account when you set the standard baseline on the measurements that have been used.

But I'd just think it's important that there be a

statement, you know, recognizing that is an indication of how you go about it.

ADVISORY COMMITTEE MEMBER HAMMOND: I think one of the problems here is that, as far as I know, this is the closest I've ever seen a standard set to whether it's about health effects. I don't see any margin of safety at all. In your presentation, Bart, I was hearing you say health effects were observed below .070. You know, so there's like no margin of safety. Normally, there's a margin of safety there for the measurement error around the measurements made is usually minor compared to when the standard has been set. And this is kind of where the problem, I think, lies you know.

ADVISORY COMMITTEE MEMBER GREEN: I'll make one point that if it's on the list of things for the next say 5 years of reviewing and research, I would expect a dedicated effort on those instruments to be able to narrow that 95 percent confidence interval by at least a factor of 2 maybe much more, and get the measurements down reliably to 1 PPB that would, I think, be useful in the future attainment. I do analytical measurements all the time, and it's amazing how I'll suddenly realize that things are 10 times more sensitive than they were just a few years ago.

If the effort is made, I bet it can be done.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: Okay. Actually, that's a good comment, because when we talked to our monitoring staff as well, they told us that, you know, at one point we had plus or minus 15 percent that we brought down to less than 10 percent the goal in the near future -- I mean, within the next year is plus or minus 7 percent. And the goal would even be more than that. So I think you're very correct.

CHAIRPERSON KLEINMAN: One other minor point is that in the standard we're talking about in an 8-hour average at that level of high precision and most of the calibrations generally don't take 8 hours to get a data point. So the actual precision of the measurements that go into the 8-hour average are probably much better than the precision you get from the calibration curves that you're measuring. And I think that's another point that really ought to be added to the discussion.

So it's not as bad as it sounds at first blush. I think we've got about an hour before the lunch break, I'd like to keep going unless there are, you know, tremendous objections to this. If people want to, you know, just grab coffee or -- there is no coffee. So we'll just -- oh, there is coffee. If people want to get up and grab coffee during the discussion, I think that's okay, but I wanted to reserve, you know, a substantial amount of

time to talk about the chamber studies. I think that's -- since that's a major basis for the standard.

And so I'd like Bill Adams to lead off with his discussion of that, and then the rest of us can chime in.

ADVISORY COMMITTEE MEMBER ADAMS: Well, I'd like to commend the staff, and particularly for what I think is a very extensive, complete treatment of the human exposure studies on ozone over a prolonged period of time.

I have a couple of minor additions that I'd like to talk about.

One is that you've used the terminology respiratory symptoms or respiratory irritation. And I'm not sure that there's very clear evidence that there's an interference of ozone due to ozone inhalation on gas exchange. I think we're talking about ventilatory effect. And I prefer the terminology breathing discomfort, indicating an effect on the movement of air. And its consequence if it's severe enough could cause respiratory irritation. But I think that looking at that maybe we should debate it, but I think it needs to be looked at.

The issue of repeated ozone exposure that is several consecutive days relative to what happens on the initial exposure where there's a significant impact going on pulmonary function and symptoms. And then how those relate to prolonged -- excuse me, how those might relate

to health effects, that I think is mentioned in your reply to commenters. In fact, it's not mentioned, it's actually analyzed in an effective way, which does not appear, I believe, in the summary statement on pages 209 through 213.

Once again, I don't have a great deal to say specifically about this, other than to say that the treatment is very complete. I think it's even. And it's explicit in the way that it's stated. And I think that the points of emphasis are very well made in general.

Now, in these human exposure studies there's certain issues that are raised, which I don't feel necessarily competent to pass on the review, others though that I do. And I would say roughly it's about two-thirds maybe 70 percent of the material over what really amounts to about 170 pages. It's maybe about two-thirds of that I feel competent in evaluating and very impressed with the thoroughness and the message that's delivered.

And in the summary statement on pages 209 through 213 for the most part it really deals with the issues that are the most critical. It distills the message that over 170 pages could easily get lost from time to time. It distills it very nicely. And that's the extent of my initial comments.

CHAIRPERSON KLEINMAN: Thank you. I'd like to

open it up to the rest of the panel for any additional comments.

I had, you know, a few minor questions, especially relating to the issue of the square wave versus the peak exposure. Admittedly this is not an area where there's been a tremendous amount of research done. Certainly, in the future, you know, perhaps more research can be done on the effects of peak exposures. But there were a few things in the document at various points that alluded to a non-linear response to ozone in terms of concentration.

And the graphs that Dr. Ostro showed where you could see the effects on pulmonary function, for example, as a function of exposure versus the different concentrations as you got to the higher concentrations, the variation from control levels got greater and greater. And, certainly it did not increase in any sort of linear fashion.

And this has been seen in other literature. The issue of whether the best measurement of the exposure is concentration times exposure times ventilation time, which is a very, you know, simplified view. It doesn't take into account the fact that there is this increasing effect of concentration.

And the reason I bring this up is I think it's

important in as we look at whether the standard is appropriately set, that this escalation and, in fact, people have looked at it normally, and so there's a -- the effect of concentration is some sort of power function. It goes up not quite square on something approximately the square of concentration times limitation times duration is more close to a linear relationship than concentration per se.

What that means is that as we look at the effect of dose through exposure estimates, the dose response will tend to drop off as a function of -- as a dose -- as it totally drops, the dose -- I think the net result is that if you average things out, we might tend to underestimate effects, and therefore there is a certain margin of safety incorporated in the way the standard is seen and the way you look at the health data, by not taking into account this additional escalation factor.

So the standard -- I think it should be just mentioned in that discussion that the standard does have some degree of protection and margin of safety, by just the way it's been calculated.

ADVISORY COMMITTEE MEMBER DELFINO: And just to add to that, Mike. Our intrinsic defense mechanisms, like anti-oxidant defense mechanisms, they're different between individuals. And one of the major points Bart made was

that there are susceptible populations. And a lot of these susceptibility factors we don't know about, unlike say asthma.

And they may have to do with post factors, genetic, metabolic and nutritional. You know, so underlying that non-linear dose response curve is the point that which the anti-oxidant stress mechanisms begin to fail, begin to become overwhelmed. So again that margin of protection, in fact, there should be a biological basis for it.

There's maybe not a lot of data, but there is some data, at least for particles and things.

ADVISORY COMMITTEE MEMBER ADAMS: I think that there is a place, I believe it's in the response to comments for letters written response to comments from others, where you folks make a statement that the effect of those particular linear terms of the ozone concentration being the most important of the 3 determinants is shown in the study in which we compared a group of individuals undergoing a 2-hour exposure at a certain level of ozone versus a 6.6-hour exposure at a lower level.

And yet the total dose of total dose is the same, and yet the FEV1 response was 3 times greater at the higher ozone concentration. It seems to me that maybe the

effective dose section of your summary that you might make a little more of an emphasis. You have said that the ozone concentrations is the most important of the determinants, that it might be -- may be a little bit more definitively as to what I just said.

CHAIRPERSON KLEINMAN: One other side comment in Dr. Ostro's presentation he mentioned that there had been less interest in the scientific community for ozone studies. And I just thought it was important to emphasize that in order to do studies one needs support. And there has been less interest in support of ozone studies by agencies, unless those ozone studies were somehow accompanied through particle studies over 10 years.

And so there has been an decrease in the emphasis on ozone research, which I don't think is due to a lack of scientific curiosity. But I think one of the issues that we do need to make in our response or our evaluation, in terms of future research, is that there really are very important questions about ozone and ozone toxicology that need to be addressed. And it may be important to look at that in the absence of just the acute effects of mortality, which seems to drive overall PM exposures.

When you look at that and you begin controlling for PM that there are fairly major benefits associated in the quality, which means it's a lot easier to discuss when

you're spending money on doing the research on that. Whereas, Dr. Ostro pointed out there are relatively fewer, much fewer, mortality incidents associated with ozone exposure, and, in fact, our ability to really see ozone mortality in the face of the larger effect of PM is difficult.

And so there has been less interest, but it's not really a lack of curiosity or a lack of scientific need. I just thought I'd throw that out are there.

Any other comments related to the chamber studies?

ADVISORY COMMITTEE MEMBER ADAMS: One other issue which you might want to look at in your summary to make the point clear, is that there now have been done not only in the square root exposures, let's say .08 but by doing triangular exposures over the 6.6 hours have the same total dose of ozone over that entire period. But it's delivered starting off at a lower concentration .08 and rising up to, in some instances, .15 in the middle and then coming back down to 0, but averaging .08.

And what's been found is that at the end of the 6.6-hour exposure there's no significant difference between the pulmonary function and the breathing dysfunction comfort. Between the 2 exposure profiles they're significantly different at the beginning, but not

between each other.

What's very interesting though is that when you get this higher peak in the middle, it initiates the significant pulmonary function and breathing discomfort earlier so that this person is in distress, if you will, sooner and over a longer period of time. I think that's an important consideration.

DR. DRECHSLER: That's an important point. The data from -- there are 2 papers that address a variable concentration profile. And they both support the view that the dose -- along with other literature as well, but dose rate is extremely important. And the observation from the 2 variable rate papers that although the end responses were very similar between the 2 concentration profiles, during -- shortly after the peak concentration time and the exposure, the effects were actually larger with some recovery by the end.

And that was one of the reasons that we were recommending the 2 standards there.

ADVISORY COMMITTEE MEMBER ADAMS: Yeah, I think that literature supports that contention, and it's valid.

CHAIRPERSON KLEINMAN: Another point to consider is that when these chamber studies are done almost all of them involve exercise, the ones that showed significant effects, but the exercise is often not continuous. Often

the studies have intermittent periods of exercise. And so, we really don't have a square wave per se. It's more of a sawtooth or up and down, because people start to exercise, their ventilation increases, but not instantaneously. They get up to a certain static level of exercise over a 15-minute period and then they stop and their respiration slowly recovers back to normal.

So that really some of the studies that have been pointed out as being continuous exposure, in terms of dose are really more of a series of spikes.

ADVISORY COMMITTEE MEMBER ADAMS: That's true, Mike, in terms of the 2-hour intermittent exercise exposures. But in the 6.6-hour exposures have been 50 minutes of exercise with only 10 minutes of rest every hour with a 30-minute lunch break in the middle.

So true to an extent, but not nearly as up and down as the 2-hour intermittent exercise exposures, which were 15 minutes of exercise, 15 minutes of rest, et cetera through the 2-hour period.

So I think it's less true of the prolonged exposures at the lower ozone concentrations, which is what we're focusing on here.

CHAIRPERSON KLEINMAN: That's a very good point. The other issues, let's see, relating to -- they're not chamber studies per se. And I'm not sure whether it's

appropriate to talk about the summary camp studies that were done where there are more of a sort of a field semi-clinical sort of setting.

Just to get a sense, is it more appropriate to talk about those when we discuss epidemiology in general or --

ADVISORY COMMITTEE MEMBER ADAMS: I think so.

ADVISORY COMMITTEE MEMBER DELFINO: Probably, because -- and the issues in the epidemiologic studies also relate to exposure assessment too. So, yeah.

CHAIRPERSON KLEINMAN: Are there any other discussion points about the chamber work?

ADVISORY COMMITTEE MEMBER ADAMS: I think there's one other issue that embarrassingly I haven't followed through on in the last few months, as I've taken my retirement too seriously, and that is that there's a very small amount of data comparing what happens to individuals that are exposed to .08 parts per million as opposed to .04 and .06.

And I have recently completed a study where individuals acting as their own controls, both males and females, were exposed to filtered air to .04 to .06 and to .08. And we found that there was a significant effect on symptoms of pulmonary function at the .08 level, but there was no significant difference between the filtered air .04

or .06 exposures.

Numerically, there was a trend towards moving in a direction that you would expect, but it was not statistically significant, not even close.

The point being that it would be nice if I finally got that off my desk and into the publishing scene.

DR. DRECHSLER: Did you look the variability between the individuals in their responses of the different concentrations?

ADVISORY COMMITTEE MEMBER ADAMS: I have not looked at that. I think that's a very critical issue. I do have in a final report in that particular study a comparison of the EPA in my own studies that several of them at .08 parts per million. And the proportion of individuals that have an FEV1 response of 10 percent or higher has varied anywhere from about 19 percent to 36 percent in one EPA study. But the average is very close to what you showed -- somebody showed here this morning.

That is about one-quarter of individuals, these are healthy, strong males, young adult males and females, about 25 percent are showing a 10 percent or greater FEV1 response after 6.6 hours exposure to .08 parts per million.

DR. DRECHSLER: What about the other lower

concentrations?

ADVISORY COMMITTEE MEMBER ADAMS: I haven't looked at that. That's a good question to evaluate. Especially, given the fact that I saw no group mean significant responses in the varying symptoms nor in pulmonary function at the .04 or .06 level.

But I did see in that group of individuals again about 25 percent that had a 10 percent or greater response in FEV1 at the .08 level. I did not look at the .04 or .06 level.

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: One of your papers that was not published that we got from you.

ADVISORY COMMITTEE MEMBER ADAMS: The one I've just been talking about has not been published.

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: I mean, you actually say in that paper that 5 of the 30 people at .06 had a greater than -- I think you said -- had a greater than 10 percent or significant changes there.

ADVISORY COMMITTEE MEMBER ADAMS: I might have said that. I guess I've been enjoying my grandson too much there in Albuquerque, because I'd forgotten that. But I do have that report with me. I'll go back and check on that.

Thank you.

ADVISORY COMMITTEE MEMBER HAMMOND: I think that's an important point that we not always look at summary data, especially given -- that we know there's variability in response. And so there's a significant -- and you're starting out, as you said, with a very healthy population, with not knowing the known susceptibilities. And even within that, there's a subpopulation.

ADVISORY COMMITTEE MEMBER ADAMS: Yeah. For example they're screened for no history of asthma.

ADVISORY COMMITTEE MEMBER HAMMOND: Right. So I think it's very important.

ADVISORY COMMITTEE MEMBER ADAMS: No significant allergies, et cetera.

ADVISORY COMMITTEE MEMBER HAMMOND: So the way we look at the data is critical as well as -- I mean, not summarize it too much, but look at it on the individual level, which I think, Bart, you had said earlier, too.

CHAIRPERSON KLEINMAN: Another issue that's sort of associated with that, and I think was alluded to in Bart's presentation, was that the percent of individuals that respond to ozone increases with increasing dose. And conversely then, the percent of individuals in a given population that are responders will diminish as you get down with lower and lower doses.

And what that really means in terms of a practical sense is that we need to take into account what is the likelihood of seeing, say at .04, maybe only 1 percent of the population in your study is going to respond. And the odds are that if we look at that as sort of a rare event an accounting statistic we've got --

ADVISORY COMMITTEE MEMBER ADAMS: Add you have to look also at air, because there is variability in pulmonary function response over time that is an external pollutant ingestion per se.

CHAIRPERSON KLEINMAN: So there's noise as well. And so I guess the point I'm making here is even if you were to say that you did not see a significant effect at that lower concentration, that's not to say if you took a much larger population to study, and were imminent in the number of people you could study in a chamber study, you know, years of -- I mean some us have done that.

But there's a limitation to, you know, precision with which we can actually measure the responses. And as we get down to if it's only 1 percent of the responding poplution -- of the population responding, you really need to have, you know, sample sizes on the order of, you know, hundreds, getting into semi-epidemiology type of studies, or you need to look at moving time.

ADVISORY COMMITTEE MEMBER PLATZKER: I'm sort of

interested. Much of the studies that show peak flows show FEV1, what about FEF25/75 or FEF75, which may be more sensitive measures of medium to small airway function.

In pediatrics FEV1 has a very, very, very high variability because of the difficulty children have in initiating forced exhalation. So we very frequently use FEF25/75 and FEF -- in my lab we use the maximal flow of 60 percent -- actually 60 percent of the final capacity has been exhaled. But I'd love to see other measurements to see whether the correlations are better than FEV1. This is in children.

ADVISORY COMMITTEE MEMBER DELFINO: That's a really good point. I think in the review you talk about the Balmes -- there's a series of studies by the John Balmes group. And they did look at mid-flows and found in fact the he mid-flows were considerably more informative. These were ozone studies. Long-term ozone studies.

So there is some data, and it's fairly limited. We're beginning to look at mid-flows as well and focusing on that. The variability is quite high, but in a clinical setting of course you have more control over that.

ADVISORY COMMITTEE MEMBER PLATZKER: We've studied children using infant lung function studies. And then subsequently pediatric spirometry and we found that if you use Vmax FRC as a measurement of maximal flow in

infants, that correlates much better with FEF25/75. And I think there should be more attention to if you're going to do just spirometry and not body, the are other parameters that might be more accurate.

ADVISORY COMMITTEE MEMBER ADAMS: About the last 5 years there's been a concerted effort to use FEF25/75. And I'm not sure again whether that is covered in the document per se. But I know that in some way in the material that I've looked at that you have, that a particularly revealing study was done about 4, 5 years ago maybe. I don't remember the name of it right now, and found that the FEF25/75 was there.

ADVISORY COMMITTEE MEMBER DELFINO: It's Skinner et al on critical care medicine. That was the Balmes study. It was an HEI funded study. It was a clinical study, and they very carefully looked at mid-flows and that's the one I was referring to.

ADVISORY COMMITTEE MEMBER ADAMS: Was that the one in which they did repeated exposures?

ADVISORY COMMITTEE MEMBER DELFINO: Again, I think it was the new sort of 6.6-hour exposure protocol with exercise. I can dig up that reference.

DR. DRECHSLER: I have it.

ADVISORY COMMITTEE MEMBER DELFINO: It's also an HEI report.

DR. DRECHSLER: There are quite a few of the human studies that have reported data on FEF25/75 and a few of the other flow measurements.

Most of the papers concentrate primarily on FEV1, because at least in the adults it has the smallest variability. Most of the FEF25/75 results are very similar to the FEV1 results.

ADVISORY COMMITTEE MEMBER PLATZKER: That won't be true in children.

DR. DRECHSLER: Right. There is very little data on children in here for controlled studies.

ADVISORY COMMITTEE MEMBER DELFINO: We just actually had about 125 asthmatic kids come through the clinic. And we did a reversibility. Of course, you know, we knew they had asthma. There was no question they had asthma, but a lot of them the FEV1, and I'm sure you've seen this in practice, was not reversible with beta-agonists. It was -- you know it was kind of -- to me it was surprising because I don't -- you know, I'm not into clinical practice anymore.

But FEF25/57 did. And it was actually very dramatic the difference between the 2. So I would agree with him. I think it's very important to start looking at that.

And just to add that exhaled nitric oxide is more

and more becoming a clinical tool to investigate asthma severity. And it's probably a lot more sensitive than the standard lung function measurements.

CHAIRPERSON KLEINMAN: I was just going to say that in looking at the literature on clinical studies, very often many measures in pulmonary function are reported. And the reason there has been an emphasis on FEV1 is that, at least in adults, it is the indicator that seems to give the most robust significance level. We came to see more significant responses to ozone in other things when we look at the FEV1 channel, but that's not to say that that's necessarily the right for --

ADVISORY COMMITTEE MEMBER DELFINO: It's an important statistically because of the variability issue. It's -- you know, when you do repeated spirometry measurements, you see much more variability in mid-flows. And it's just because the nature of how the maneuver is done, which is why, you know, things like E&O are much more stable than nitric oxide when they're done properly in a clinic setting.

ADVISORY COMMITTEE MEMBER HAMMOND: You know, I would also like to weigh in on the looking at the mid-flow range, because we've actually faced this in the Asthmatic Children's Environment Study. We're also finding that to be particularly an important thing to be looking at

statistically. So that I think that's kind of maybe the future for children. It's important to be looking at those.

ADVISORY COMMITTEE MEMBER FANUCCHI: I'd like to say I think one of the problems that we're having here is that the people that have been dealing with children's health issues and looking at lung function and lung development in children realize that children are not little adults.

You laugh, but we come across this over and over and over again. You can't treat it as a tiny little adult. Their architecture is very different. Their lung does not grow symmetrically. They have different gas exchange -- the alveoli. The gas exchange area of the lungs is continuing to develop throughout childhood. Cell populations are different, so the target for ozone may be different in a child than in an adult.

Again, looking at the mid-flow versus the FEV1 is a good indicator that we have to readjust our thinking if we're interested in protecting the children from adverse health effects.

CHAIRPERSON KLEINMAN: Any other comments?

ADVISORY COMMITTEE MEMBER PLATZKER: I'd like to just say that I think in children also, if you're looking at small effects, you may have to exercise children to

really see that. We've studied 2 groups of children who had infant-related injury to the lung and actually 3 groups now. And at 10 or 11 years of age -- the average child was just about 10 -- we found the most significant long-term effects were found by looking at exercise stress testing. And actually post-exercise airway obstruction.

CHAIRPERSON KLEINMAN: So there are certainly research recommendations that should be added to our compilation relating to this issue.

I'd like to open it back up to any, you know -- are there any other questions for the staff or are there discussion points that we want to make on any of the topics we've touched upon this morning so far?

Because if not, I think it would be worthwhile on this point to break a little bit early for lunch, and that will give our committee a little bit extra time to caucus and discuss exactly and summarize what we've gotten so far.

And so I'd like to adjourn until 2 o'clock if that's possible.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: That's sounds like a good idea.

CHAIRPERSON KLEINMAN: Okay. Then we are adjourned until 2 o'clock.

(Thereupon a lunch break was taken.)

AFTERNOON SESSION

CHAIRPERSON KLEINMAN: Ladies and gentlemen, I'd like to try and reconvene. So if everybody could find your seats, that would be great.

I just wanted to -- in terms of just sort of a housekeeping sort of issue, we have for the Committee a room set aside for dinner. And it will a be a working dinner. And I've been told that the room should be available to us by 6 o'clock. So from 6 o'clock to roughly 7:30, for those of you who are looking to escape and get off by yourselves somewhere. But that's sort of the timeframe that we'll have for our working dinner.

Again, I wanted to thank everybody for coming. And I wanted to welcome Henry Gong, one of our newest members of the Air Resources Board, who just came; and Shankar Prasad, who's the Health Officer at the ARB. So welcome.

And are there -- oh, someone sent or requested a 68-page fax. And Sue has it. I don't know whose it is, but it will be on the table.

As if there wasn't enough information to be read. I turned it down immediately.

Okay. During the coffee break somebody can read it and give us a brief review.

We're going to move on with the review, unless

there are some questions from this morning that after reflection people want to raise. I don't think there were.

Then let's start with the epidemiology section. And I'm going to ask Ralph Delfino to lead off on that.

ADVISORY COMMITTEE MEMBER DELFINO: Yeah. I thought the section was very well written and very comprehensive. Quite impressive. And I also thought that it was very fair and clear in pointing out a lot of the methodological weaknesses.

So I think my contribution here will really be to maybe try to fine tune some of the -- some of the issues with regard to the methodologic weaknesses and how they might affect our interpretation of ozone health effects using epidemiologic data. And to also add a few studies that were -- a few key studies that were missed; understandable, given the, as Mike previously stated, the vast number of studies.

The ones that should not be missed though for sure are any of the epi studies conducted recently in California. No matter how small, I think it's important to recognize that although ozone's the same everywhere, it's quite conceivable that ozone in California may have a different effect across regions depending on exposure misclassification and correlated air pollutants.

Sulfate might be strongly correlated with ozone on the East Coast but not here, for instance. Whereas here ultrafine particles in the L.A. Basin has been moderately correlated with ozone and is photochemically generated presumably because of that -- as a result of studies that have looked at that from the Southern California Particle Center.

So I think we have some different issues with regard to ozone as an indicator -- again, back to that word "indicator" -- here in California versus many other parts of the country.

So that said, interpreting the studies in California, I think it's important to interpret them based upon the regions in which they were conducted. And in particular looking at inland regions of California where -- I mean you have a temperature gradient, as you know, from the coast inland of 20 to 30 degrees in the summer increase in temperature and of course much higher ozone. And as a result of the high outdoor ambient temperature people tend to spend, including children, more time indoors, they use airconditioning, there's less -- and all these things were of course well described I think in the exposure section, but need to sort of be brought forward briefly, but brought forward into the interpretation of the epidemiologic data in particular,

again those that have used regions of study where high temperature might have influenced the exposure to ozone and induced more exposure misclassification than areas closer to the coast.

And in my written summary I'd mentioned a couple of -- several of the studies that came to my mind. My own studies of course were -- most of them have been conducted inland where it's very hot. Often times we don't see an association with ozone, sometimes we do. And an indication of why there is no association is that, if you look at the correlation between personal temperature, that is, temperature gauges worn by people, by the kids, by the asthmatic children, and ambient ozone, it tends to be no correlation, very low, .1. If you look at the correlation between temperature at the ambient side, of course it's always pretty high, so at least moderately correlated.

And we all know about exposure misclassification with ozone.

So I think it's really critical -- in particular Seventh Day Adventist cohort study has regions inland where it might have impacted their results.

And the big one of course is the children's health study. In a text reviewing the study by McConnell, which is I think a very important study in southern California, where they found -- in fact although looking

across all the kids -- and these are nonasthmatic, you know, basically a general population sample, and they saw no association. But then when they looked at kids who were engaged in three or more sports, they found an association in high ozone communities.

And of course those high ozone communities were inland communities. So if you think about it for a little while -- and what was said in the text was it only referred to effect modification by physical activity. I think it's really important to really fully interpret that, in saying that: Why does it affect modification? Well, it's because they're playing three or more sports, getting a higher dose, and probably most of those sports are played outdoors.

So if they're living in these hotter areas, they're outdoors exercising in the ozone, so to speak. And the magnitude of exposure misclassification for these children, that subset of the children's health study, is much less than the rest. And I believe the McConnell paper actually talks about that, you know, in the body of the conclusions or the discussion section of that paper.

The other children's health study that is probably severely impacted by this issue is the study of lung function growth. You discussed the Gauderman 2000 paper, which is the four-year follow-up for fourth

graders. I would actually just briefly mention that paper and actually summarize the follow-up, which was the eight-year follow-up published in the New England Journal of the same cohort, with dropout, for eight years. In other words they followed him right straight through high school.

And very similar findings, but considerably more robust.

And, again, in that study they found associations PM 2.5, NO2, acid aerosols, I believe, elemental carbon -- you know, all these things linked to traffic-related exposures but not ozone. Again, you know, the ozone communities are in these very hot areas like Alpine, where I've done research, and near Rubidoux and all that in Riverside County. So I think those results need to be carefully interpreted.

They did not -- and I assume they're going to do probably more publications. They did not stratify in this particular case on outdoor activities. They do have that data. So I kind of expect a follow-up publication on that. Where indeed we might see an effect on lung function growth in children who spend more time outdoors either because of sports or whatever.

I thought the review was very fair in terms of talking about -- in reference to the time series studies

anyway, the excessive control of temperature and how that might actually, you know, basically eliminate the effects of ozone, particularly where seasons are not analyzed separately, where, you know, you lump summer in with winter and use all these smoothing filters and so forth. I never thought that was a way to analyze time series data, and I always questioned that, for ozone in particular. Maybe not so much particles, although that's another story. So I think you did very well on that.

I would just -- just an organizational issue. Those problems apply to all study designs, not simply the time series. So the cohort studies, the panel studies, it applies to all of them because -- actually not the cohort studies, but the panel studies where you have repeated measures.

So the control of temperature is a real problem. We find that when we control personal temperature, there's no association between personal temperature and any of the asthma outcomes.

So you make a good point. And I would just reiterate a very good point, that these weather variables, there's very little, very little physiologic data to suggest that temperature or relative humidity by itself is necessarily an important -- are important factors on the outcome itself.

So I think there really is excessive control.

And where studies don't present results without temperature, I have a real problem with that. In other words if they're -- the only results they present are controlling for ozone, then I think that dramatically weakens the interpretation of particularly null results.

Oh, yeah, so the other organizational issue -- you did talk about misclassification of ozone in relation to -- this personal exposure misclassification in relation to time series size. But that really applies again to all study design. So just an organizational issue. Maybe all those weaknesses should be put up front because they apply to all the study designs.

And in my written summary I talk about some of the papers that weren't mentioned. A series of studies that also looked at the effect modification of antiinflammatory medication use in asthmatics. You mentioned one paper I think that -- by Gent on that issue. Kids that are taking maintenance medication, largely inhaled corticosteroids, are going to be more severe asthmatics.

On the other hand, particularly among poorer populations, who might be more exposed than the more well off part of the population, a lot of those kids do not receive these maintenance medications. And so they may be

persistent asthmatics that are unprotected, so to speak. So they may be in fact more susceptible to air pollutants than the kids that are on inhaled corticosteroids, who in some of these studies show a stronger association. But others such as the ones that I've published don't.

And one of studies that was not cited that should be actually is the study from Ira Tager's group. Kathleen Mortimer is the lead author from the Inner-city Asthma Study. Looking directly at the effects of ozone on inner-city kids with asthma. And they did find significant inverse associations with peak flow and associations with strong -- with symptoms.

And it really pointed -- and the Mortimer paper is very clear on the susceptible population issues, and that they really did a great job of looking at susceptible -- they had the power to look at different susceptible populations, and they found that -- getting to your issue about premature infants, they showed the strongest association with ozone compared with the rest of the group, low birth weight or premature infants.

And of course all these kids lived in low income neighborhoods. And they were one of the other studies that looked at medication use and in fact found weak -- very weak or no associations for kids that were on ICS or inhaled corticosteroids, and found the strongest

associations with kids that were on Chromelin, which is a mast cell degranulator inhibitor medication. But it's not as strong an anti-inflammatory as inhaled corticosteroids. So it sort of suggests that these were kids with persistent asthma that were not well protected enough against the effects of ozone, but showed the strongest association.

A little complex, but it really again I think will help in your argument that we need to protect the most susceptible populations, and here they are, and these are the papers that have actually -- the epidemiologic papers that have actually looked at them. Again, reiterating the point the controlled studies have not been able to for ethical reasons. The epi studies can and have. And wherever there is data -- and it is limited, because unfortunately a lot of panel studies and other studies don't even look at susceptible populations -- but where it is -- where the data does exist, I think there's some pretty interesting information to cull out of there.

Again, I'm citing myself because I know my work better. We did do a study in L.A. and Hispanic children funded by ARB. And I in my written summary do show that we did find ozone effects. And those ozone effects were in a very small subgroup. Again, this is, you know, a small subgroup. But there were associations of kids with

more severe asthma symptoms. And these kids were on maintenance medications. So the mixture of effects reflects the problem of medication versus severity. And I think you talked about that fairly well.

And I have -- my written summaries cover that.

On the time series study, again I thought the discussion about the co-adjustment approach really is important. And this is something that has probably dramatically affected the time series literature in the opposite direction that the S plus debacle has; that is, that they have underestimated the effect of ozone with co-adjustment. They have underestimated the effect of ozone by not doing seasonal stratification.

I mean we -- when David Bates first did his studies, that's the way we thought it should always be done, the way David Bates did it, do it in the summer, even four seasons -- do it separately four seasons. And then people started doing these smoothing, doing the whole year all at once. And it just never made any sense to me. And the co-adjustment approach, I thought that section was just beautiful.

I concur with Dr. Bates about the Atlanta study. Really important to add that. But I would add that, yes, the ozone levels did go down when the Olympics were on and all that traffic was blocked, but a lot of other things

went down as well. You have to sort of be fair in that sense, that, you know, there's traffic exhaust toxic pollutants and particle bound toxic components that probably were dramatically reduced as well. Precursors of ozone, again, you know.

And most of my other commence are really just editorial.

And I reiterate again, I thought you did a good job of talking about the smoothing functions and time series analyses. That when you smooth temperature, you're smoothing across the midrange of temperatures that are really unlikely to have any effect on any health outcome. I mean anything below, you know, 80 degrees Fahrenheit -- or whatever -- Celsius -- I forgot since I haven't lived in Canada for a while -- probably don't mean anything. Or above a certain -- you know, a certain lower threshold of cold. You know, and it's not linear either, so there's effects at very low temperatures and there are effects at very high temperatures.

And there actually are a couple of papers -- and I forgot to put that in as well -- but showed a U function for ozone, a U-shaped association, I believe for ozone, depending on the temperature adjustment. So I thought you did a very good job at pointing that out.

And the real methodologic weaknesses, which --

you know, which don't apply as much to the PM studies. And as you pointed out and Mike pointed out, that the literature has been -- the epidemiologic literature has been so focused on PM, but these problems with ozone have been forgotten, I think.

And that's really it.

CHAIRPERSON KLEINMAN: Great. Thank you.

Let me open it up just to make sure that nobody else on the panel wants to --

ADVISORY COMMITTEE MEMBER FANUCCHI: I'd like to say something.

What I'd like to see with the epidemiology -- and I think it was a very thorough review -- is that with ozone in the nonhuman primate model we've been seeing effects of ozone on lung development at a very, very early age in the nonhuman primates, is that we can start at 30 days of age. And it's somewhere between 30 and 90 days of age where we actually see what appear to be irreversible changes to small airways, structure, smooth muscle, epithelial innervation. And what I'd like to see with the epidemiology is if there's a way to tease out -- if the history of the children is known and how long that they've been living in high ozone areas, is it since birth? Because I think that very early time point might be very important to effects later on. I know that's not an easy

thing to do and getting history is difficult.

ADVISORY COMMITTEE MEMBER DELFINO: Yeah, I can't speak for the CHS. Maybe somebody from ARB that's read all their reports can. But I don't -- there's a background questionnaire that's quite good in that study. But I really don't think -- I don't think they have a good handle on that at this point or they're not going to analyze it, try to do -- you know, retrospectively figure out where they've been and how that's affected. They've reviewed the Ira Tager study though that did.

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: Well, I can just speak to the Ira Tager's study of UC Berkeley freshman. They've already published one article. And Ira has another I think that's being refereed now. And he did -- in that he reconstructed ozone exposures into early childhood into birth -- back to birth, I think. And one of the findings -- that paper's rather difficult to get through actually.

But one of the findings was that the earlier childhood exposure did seem to have a stronger effect on long-term changes in lung function than did more recent exposures. And I think he's suggested to me that when they've redone the analysis now with I think a bigger group, they're finding that as well. So I think your

point is well taken there.

ADVISORY COMMITTEE MEMBER DELFINO: Yeah. And that study will feed into the national Children's study in a direct way, I think.

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: We have Pat Kinney here who did a similar type of study.

Did you have early childhood for that?

DR. KINNEY: We've never broken out the earliest time periods. We could do that.

We haven't -- well, I think we did split it up into sort of 0 to 6 years, 6 to 12 and then 12 to 18. And we didn't see big differences in those three categories. But we never looked at the, you know, first couple of years of life.

That was a study of about 1,700 Yale freshmen.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE:

That was Pat Kinney, by the way, who's a contractor with our -- for writing of the document.

ADVISORY COMMITTEE MEMBER PLATZKER: There's difficulty with that though. If you're going to look at the amount of exposure that the child has from birth, you really need to go back and see where the mother was during her pregnancy.

In addition, my concern with a lot of the data

that's published is that it's not good enough to say 0 to 6. If you're talking about exposure, you're talking about concentration times time times respiratory rate. And we know that the newborn breathes 40 times a minute, a child at 9 breathes 12 to 14 times a minute. The exposure is going to be a great deal more for the infant. So that the -- you have to define your population.

Second of all, my concern about a lot of the studies that look at asthma has to do with the fact that they don't really categorize the asthma. I mean we've -- we know that there's intermittent and then there's persistent, and we have three written levels of persistent. Who are the patients that we're studying? So that I think the characterization -- we may be underplaying the data -- averaging data when we should be dividing it and looking at sensitive groups.

And If you look at asthma versus other children who have either congenital anomalies of the airways and lungs or children who've experienced injury to the lung in early childhood, these children are probably an even more sensitive group who may be more sensitive to environmental pollutants. And I think we have to recognize that and worry about it.

These children appear to have ongoing inflammation in the lung, even transcending the period of

time when they were ill at birth. So that this is another very vulnerable group of patients and I think we need to have better epidemiologic data on that.

CHAIRPERSON KLEINMAN: On that point, I guess it was six years ago when the children's bill was passed. We had a review of the California standards with respect to whether they were adequately protective of children. And there was a chapter on ozone written I believe by Ira Tager and John Balmes.

And I'm wondering whether Bart or Pat would be able to tell us what the conclusions of that review were since they were comparing it at the .09 ppm one-hour standard and were retaining that standard. So I guess the question I would like to put out is: What were the overall findings at that time? And, you know, have there been significant studies considered since that review that might alter the thinking? And, if so, how is that being reflected in this document?

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: Well, I can try to address that.

I did look at that report again a couple weeks ago. And they did say -- I think they couched it in probabilistic terms, that it was based on the current studies, primarily a lot of the epi studies that there was some likelihood that children would not be protected at

that level.

I think our thinking was -- or is that by adding the eight-hour average, that we'd be affording the additional protection that's needed. And in fact if .07 is actually -- or .070 is actually attained, we shouldn't see too many exceedances or we shouldn't see any concentrations up as high as .12 ultimately for one hour up to .10.

So we think the double standards provide the protection that they were talking about.

Regarding studies since then, yeah. I mean, in the last five or six years there's been a lot of new studies, particularly the mortality studies that have come out. But a lot of the studies that you saw us citing are from the last five years or so. So there's a lot more literature in there.

But, you know, the other side of it is, again, as I've mentioned, the difficulty from the epi studies -- that does have some very distinct advantages -- but the disadvantage of not knowing exactly what the averaging time is: Is it a couple days; is it one day; is it one hour; is it eight hours, so on and so forth; it makes it harder to say something definitive of how those studies drive the actual standard as opposed to using it as a supportive number for the margin of safety.

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION MANAGER MARTY: This is Melanie Marty. I just wanted to add in other point.

That when the studies were published regarding lung function at age of 18 and also when the children's health study published the connection between ozone exposure times three or four sports, Bart -- I asked the question of Bart, "Well, what do you think the range of exposures was that those children were exposed to, especially the study that looked at lung function at 18, when those kids were young? You know, what were the concentration ranges?" And so we did have some discussion that those kids likely were exposed to pretty high concentrations of ozone compared to the standard that we're trying to set. So we did have a lot of concern about those studies and whether our eight-hour standard would be protective of those effects. And as Bart mentioned, we think that the eight-hour standard is going to be a driver and drive down those peaks.

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: I have a couple other quick responses, to Dr. Platzker first.

For sure that's a been a difficulty in terms of characterizing the asthmatic subjects that we've looked at in epi studies. I mean until Ralph came along I think my

group, Michael Lipsett and I had published the most asthma panel studies. And now Ralph is now the champion, I think. But one constant problem we have in these studies -- I think the two biggest are characterizing the population adequately; and in dealing with the medication question, whether the group of steroids are going to be protective and you won't see any symptoms -- and sometimes that's the case -- or whether people are taking them regularly. And we've actually tried to design some studies where on a daily basis we actually ask people if they were taking their preventive medication to try to get at that. So it's a very difficult issue.

So both of these things I think are one reason why we see different types of results in some of the asthma studies, the panel studies that look at symptoms every day for like two or three months, because the populations may be radically different and the medical regime compliance might be radically different.

And I think that goes to some of the things that Ralph was talking about.

But the other thing was about the seasonal splits in the time series studies. The reason that people haven't done it as a matter of course is I think simply because of power issues, that once you start filling up three years of data you start chopping up a relatively

rare outcome, like mortality or even hospitalization, into three-month periods, you really start to run into power problems that is likely to miss an effect even if one was there when the number of days that follow up become so small.

So people are looking at that more and more. But I think that's the other side of the issue.

ADVISORY COMMITTEE MEMBER DELFINO: Did the end-map study -- I'm trying to remember if they -- did they very carefully look at seasonal differences and effect?

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: You could define -- I mean you'd need to define "very carefully". But, yeah, they did look at summer season versus full year both in the original 2000 study, in the 2003 study, and then the one that came out last month, they have done that.

ADVISORY COMMITTEE MEMBER DELFINO: Because that was clearly powered enough to do that.

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: Yeah.

You know, of course they're combining 95 cities too. So that gives you -- when you do the meta-analysis you've got a lot more power to detect an effect when you combine it. And it's less likely that you're going to

find significance in a given city. So that's one of the powers of having multiple cities when you do that work.

ADVISORY COMMITTEE MEMBER FANUCCHI: One of the questions that I have is that -- we were talking about the chamber studies earlier. And the chamber studies are comprised of healthy adults stuck in chambers. The epidemiology, we've got children as best we can. But we don't have defined ozone monitoring on the children. We just have ozone at some monitoring station.

One of the things that we might want to consider for further research to help us set standards and answer this is to find a model that we feel is fairly representative of the human and do chamber studies in that model, and I think, you know, as what we talked about later, a nonhuman primate model in order to get at some of these lung development issues that we're talking about at relevant doses. Because you can't stick a baby in an ozone chamber. And the monitoring on the epidemiology is only so-so. So I think it's something to be considered in order to continue to address the issues "Is this going to be protective or not?"

CHAIRPERSON KLEINMAN: Other comments?

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE:

Dr. Kleinman, one thing I might -- Dr. Fanucchi brought up the children's health study and, you know,

whether we have data. And I'm not sure if the investigators ever did go back to look at, you know, when the kids were born and -- but they do have -- Do you think they've gotten results?

DR. DRECHSLER: I'm not sure that they did, but I don't think it's published.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE:

So with that comprehensive -- I know that we've got a comprehensive data on all those kids, because they wanted to make sure they knew where they were born, how long they lived in each of their communities. What they didn't have is of course the monitoring network for that study we started about 1993. But there are other ways you could go back and back-calculate what their exposures from other central site monitors and --

ADVISORY COMMITTEE MEMBER DELFINO: Well, there's -- that's for the PM part of the study. There should be plenty of ozone data, I would think.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE:

That's right, for the ozone data we should have --

ADVISORY COMMITTEE MEMBER DELFINO: Or for all those areas.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE:

And we have an extremely comprehensive ozone

network in southern California. So that's something we'd bring up.

ADVISORY COMMITTEE MEMBER FANUCCHI: Right. Because I think that the experimental data is showing that there's a very early window. When the lung is differentiating and developing, that it's setting its own baseline for all sorts of systems within the lung. And if you disrupt that development, you won't end up with the same baseline. So you'll end up with an altered lung development no matter what. And which you may or may not be able to tease out later if you don't go back and look at what happened early on.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: Right.

Okay. We'll check into that.

ADVISORY COMMITTEE MEMBER PLATZKER: One other comment in support of your epidemiologic section. You know, the studies that look at change in lung function and children spending time outdoors in three different sports, clearly they wouldn't be participating in three different sports if they were that vulnerable and at high risk of having problems. So that this may be really just the tip of the iceberg. They show changes -- the people that -- the children who are more sedentary are likely to have much more provocative changes in lung function.

CHAIRPERSON KLEINMAN: I don't remember the details of that study. But the implication was that when they looked at kids who did less activity, they had fewer --

ADVISORY COMMITTEE MEMBER DELFINO: It was risk of asthma onset --

CHAIRPERSON KLEINMAN: -- risk of asthma onset.

ADVISORY COMMITTEE MEMBER DELFINO: -- was the outcome.

CHAIRPERSON KLEINMAN: So it --

ADVISORY COMMITTEE MEMBER PLATZKER: But not pulmonary function? That was a different study --

CHAIRPERSON KLEINMAN: No, that would be different.

ADVISORY COMMITTEE MEMBER DELFINO: Yeah, the pulmonary -- the lung growth and pulmonary function, they did not -- they didn't report that strata -- that stratification or that stratified analysis in the New England Journal paper.

So that's why I was saying it would be nice to have that data to see whether there was a change in lung function. And, again, if they did, then that would be a concern.

But still I think his comment applies. Asthma onset, you know, you'd have to think about

exercise-induced asthma in that particular scenario of three sports.

CHAIRPERSON KLEINMAN: Which kind of leads us into the topic of mechanisms and toxicology.

So I'd like Michelle to lead off.

ADVISORY COMMITTEE MEMBER FANUCCHI: Actually, again, I thought it was a very comprehensive chapter, with a lot of data put into it.

I took to heart the charge that we were to look at whether or not this was going to protect children and infants and was that clear and transparent. And I think that, from an organizational standpoint, it could be made more clear. And it might actually help the case for the standard using the same information that's there.

But one of the first things that Chapter 11 left out -- it talked a lot about mechanisms of toxicology as far as inflammation, but it didn't talk about mechanisms of toxicology of injury by chemical defenses, anti-oxidant defenses. And one of the things that's very different between young children, infants and adults are their anti-oxidant status. And normally children have very high levels of anti-oxidant enzymes. However, they're still susceptible to ozone injury. And that's shown in laboratory animals and in the nonhuman primate models.

And so I think a section that compares and

contrasts the development of those systems -- and in my written part I put down a few of the articles that could be considered for that -- one thing you have to take in mind with some of the older literature looking at anti-oxidant enzymes is that they've done lung lavages and so it's not a sight specific, it's a whole airway level, and so it may wash out some of the effects. But there's definitely a difference between children and adults.

The rest of the chapter I thought was really well written. I do think though that if you reorganized it so that with each question you put the children's information in contrast or comparison to the adult information, it would give us a better feel for whether or not children are more or less susceptible in any particular area.

And one of the things I noticed in the comments from people is that the section that discussed the nonhuman primate model, the allergic asthma model, that section confused some of the public in their comments. And one of the things that I think that would help that section is some of the information on the lung development of those monkeys that were exposed to ozone only would be moved into the other sections of that chapter and tease out really what were ozone-only effects on lung development during that time. And then later on add in what happens when you add an allergic situation over the

top of that. And I think that would make it very, very clear as to what effects ozone may have on lung development, epithelial innervation, smooth muscle development.

There's also a study that came out of that that shows that ozone during postnatal developmental alters CMS effects. And so that could affect pulmonary function or ventilatory rates.

But, overall, I thought it was a nice chapter.

I don't know if you had any other comments.

ADVISORY COMMITTEE MEMBER SHERWIN: I think I'll save my comments.

CHAIRPERSON KLEINMAN: The point that was just raised in terms of mechanisms of defense, which are just not really covered in the document, are important because, at least judging from some of the in vitro studies and some of the other mechanistic studies that are done, there appears to be a stratified sort of response that first causes a stimulation. At low doses you increase or up-regulate some of the anti-oxidant mechanisms. And then at higher doses you begin to overwhelm those and then you begin to see injury.

And this may be partially responsible or at least play a role in that nonlinear dose response model. And I think it's important to at least mention that in the

discussion of mechanisms, because it does, you know, in turn, support, you know, some of the other questions of how you're looking at the data and projecting it back to set a standard.

Even though you don't use the in vitro data or the animal data per se as your hard and standing setting process, I think it is a useful, you know, substantiation of that.

Another issue that came up in our discussions at lunch were the locations of where ozone actually has its effect, which may be different between the developing lung and the adult lung. And I believe, you know, that there's somewhat known about deposition of ozone from Ozone 18 studies. I don't know if any have been done with juvenile animals. But I guess the question is: If there are data on that, can we -- you know, is there some way to use that data to help understand some of the mechanistic issues and differences between the child and the adult?

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION MANAGER MARTY: We did have a little bit of discussion in Appendix A of the anti-oxidant defense. We can elaborate on that and pull it forward to the main part of the document.

ADVISORY COMMITTEE MEMBER FANUCCHI: That would be helpful.

I think what Dr. Kleinman was maybe alluding to was some of the ozone dosimetry work that's been done. And we were wondering if Dr. Plopper wanted to come up and talk about -- we were talking about location of ozone injury and whether or not there were any studies besides the Ozone 18 that were discussed in here that would help understand the air flow or maybe the deposition target locations in juveniles versus adults. And since you're an author on the document.

DR. PLOPPER: I think the main issue here in terms of deposition of the ozone is understand the three-dimensional architecture of the airways. And the data that's out there's almost minimal for experimental studies. I mean the problem is knowing when they change.

The data that's there says that it's a very linear pattern, but it's done by summation of large numbers of -- based on generation of branching.

And there's one study out there that shows that if -- once you get past the third generation you're talking about, it's close to twofold orders of magnitude differences in sizes for the same airway generation. So lumping them together is not going to help us understand this. And I don't think there -- at the current time there is any really good literature that actually defines what the problem is.

But I can tell you that we have two studies out now that show that for a limited number of airway generations during postnatal growth, especially probably within the first two years, that any specific airway generation is not going to grow in a linear fashion. And what this means is that the differences in resistance to air flow for even two neighboring airways of different sizes in adults will be such that the air flow pattern's very likely to change very quickly.

So I don't know if that answers your question. But I don't believe there's anybody's ever done a deposition study for oxidant reactants in infants.

But the pathology would suggest that there's some differences in distribution of the pattern versus adults. They're certainly more susceptible.

And the other confounding thing, which since I'm here I will emphasize, is the fact that it appears that during these phases of growth they're highly susceptible to disruption by inflammation and injury, which means that they don't grow the same, which means that the actual architectural organization of a child that grew up in a heavily polluted area like Mexico City or Los Angeles is going to be very different than one that didn't.

And that means that -- probably the other thing it means, that depending on the level of pollution when

they were growing up, that when they get to be adults, the architecture's going to be different, so you can't even compare adults at any particular time or juveniles with younger children as a baseline because they had a different ozone history.

I don't know if that answers your question.

ADVISORY COMMITTEE MEMBER PLATZKER: Given the smaller airways of male infants versus females, is there a difference?

DR. PLOPPER: I would like to know that. But I don't think that data's ever been out there.

What's available in the literature's virtually all done on males.

CHAIRPERSON KLEINMAN: Yeah. I raise the point, you know, not just because it's esoteric and interesting, but also because this is, you know, one of the few pieces of evidence that we've got where we're linking pulmonary function changes, which are somewhat ephemeral, to real architectural changes, permanent changes in the lung structure.

So it's not just -- you know, for example, if this can be analogized to the children's study where they're showing the kids growing up have lower lung function in dirtier cities than cleaner cities. This is not just the fact that they don't breathe as hard or, you

know, there's some voluntary aspect or muscular aspect to it. There's an architectural difference, which is unlikely to be improved. And I think that's very important when we start to evaluate the importance of, you know, lung function changes as one of the things we use in the standard-setting process.

DR. PLOPPER: I'll agree with that. Some of our monkey studies show that the average airway generation loss is between three and six if the exposed is infants. Which means that the architecture's completely different. And it sort of fits in with that study that was done, the kids that grew up in Mexico City. They had all kinds of organizational changes in the lung by radiological measurements. And that would fit in with experimental data as well. So, yeah, I think your point's taken.

CHAIRPERSON KLEINMAN: So in terms of, you know, additional support for the scientific basis for an ozone standard, I think information like this should be explicitly included in the chapter on toxicology and mechanisms if possible. But I think it's -- thank you very much, Dr. Plopper.

Okay. Any other comments?

ADVISORY COMMITTEE MEMBER SHERWIN: Maybe at this point I would like to bring up the -- defining of an adverse health effect. I think this is a core problem.

And I think the ATS shortchanges it. And you shortchange your data and your conclusions by using it.

And the reason I say that is that the real adverse effect that we're worried about is chronic lung respiratory disease, CLRD. And CLRD is now the fourth leading cause of death. It is going to be the third very shortly. And the reason why that is doing that is it takes about 20 or 30 years for the lung to be destroyed enough to become manifest as a clinical disease.

ATS does not recognize subclinical disease. And yet that subclinical disease can be very serious. So if we turn the question around and not say, "What are the adverse influences of ozone?" Respiratory inflammation, pulmonary function abnormalities. Those are important, but it doesn't give us the real core. And the real core says 30 years before these people manifest CLRD they have lung disease. They don't know it. Their quality of life is unknown to them.

I mentioned at lunch time you can lose 70 percent of your lung and not know it. So this is an important fact.

So what we're now turning the question around is, "What influence does ozone have in causing, promoting, facilitating and exacerbating disease that's already in the lung aside from any other...?"

And to back this up our studies of young people have shown one out of four 15 to 25 to have severe respiratory lung disease -- respiratory bronchiolar disease, which is an inflammation. And we're not talking about minor things.

And I should also say to you that emphysema is ubiquitous in the adult population. We all have more than trace amounts. I don't see any human lung that I could look at and say, "Here's a normal lung." I mean they all show disease.

So now what does this say? It says that we're not asking what ozone does that's bad. We're asking if we've got something bad, what can we do to reduce that, minimize it?

So we have an opportunity to say -- we don't know what causes CLRD for the most part. Well, smoking of course. Air pollution, obviously implicated. But we don't know the cause. But here's an opportunity to say, "Well, one thing we do know. Ozone at ambient levels produces changes" -- as Charlie Plopper and other people have shown, especially the primates at .015 ppm over a period of time -- a lesion which is identical to the minimal lesion we see in young kids. So we're seeing severe -- the animal studies we've done, at higher levels than what Charlie Plopper has done, show the same basic

lesion. But it's mild. I don't see these animals.

So what I'm seeing in humans is a very severe disease. It is the precursor, I don't have any question, to whatever chronic lower respiratory disease is. We know so little about it that nobody makes a diagnosis of asthma or emphysema or chronic bronchitis anymore. Clinically you can't tell. Well, if the clinicians can't tell, how are we going to come up with signs and symptoms that relate to what ozone's doing that's bad, to asthma or emphysema, to chronic bronchitis or bronchiolitis?

So my message is, let's ask that big question of "What role is ozone playing?" And, as I say, from the studies that I know of, and especially the primate studies, as well as all the other things that have been done, and the epi studies and the chamber studies, there's no question in my mind that ozone is playing a role. Now, the only unanswered question is: What's the magnitude? What is the -- how does that compare -- if you want to rank pollutants, how does that compare to what NO2 does or how PM2.5 or PM10? So we've got a whole bunch of problems.

But because we don't know all of these, our problem is focused on ozone. We know that ozone has an adverse effect, producing a lesion we see in humans that goes into CLRD to become the fourth leading cause of

death, silently. It's clinically covert. Almost all of emphysema, for example, is covert. So is bronchitis for the most part. You know, who doesn't cough. When I was in Boston, I mean everybody had bronchitis in the wintertime.

So it got be very hazy. So my suggestion is that we turn the question of adverse health effect around to saying if we adopt these standards, which I strongly recommend -- and I think you people have done a great job in putting together the data -- will this ameliorate the problem we're facing? And I think it will. I don't know how much it will do. But it's -- we are in the position of saying we just can't let CLRD exponentially increase. They say it's leveling off, not in women but in men. I'm not sure that's true. The point is it will become the third leading cause of death very shortly.

So that was one of the things I wanted to bring out.

There are studies that should be done. And we were asked are there things we would like to see done. And I think I now can say this, because I'm at the age where I don't buy green bananas and I'm not going to be getting grants for it for five years to do it. So I would recommend that we strongly support what I would call epidemiologic autopsy studies.

What does this tell you? We have severe lung disease. We have a lot -- incidentally we have a lot of severe other diseases, like cardiovascular, for example. One of the first cases I ever saw in my military experience was a young boy, 21, dying of coronary disease, massive occlusion of one -- he already -- he had a left coronary disappear. He was only 21 years of age. And the first sign of sudden death with myocardial disease -- I beg your pardon -- the first sign of myocardial disease is sudden death in 25 percent. So this subclinical covert is being overlooked.

So I would like to see epidemiologic autopsy done, saying, look, let's find out what is the level of this damage. You can measure it. You don't have to talk about subtle findings or reversible findings. We can show you changes. For the most part you can evaluate. Some of these I suppose are reversible.

But when we see alveoli distorted, the lung gets remodeled so that you don't recognize it anymore by the time they're adult. You want to measure alveoli, you don't go to an adult lung. You just can't do it. I tried to do that in a study and I just couldn't do it.

All right. So this says why not get an inventory of good cells, good alveoli and bad ones and plot them. And if you start implementing standards that will

ameliorate this kind of lesion, you ought to be able to see it. If air has been -- if air has been improving in the South Coast Air Quality Basin -- we've got eight years -- no, we've got three years of -- no, it's eight years of material, three years recently, but eight years total material over a period of years somebody could go along and say what is the likelihood? They have to add to it. I don't want to do that study. It's just too big a study. It's like personal monitors, it's going to cost money, it's going to cost a lot of the people -- anyway.

So that's as much as I think I want to say that -- well, there's one other thing to be sure that this message gets across. We have long ago abandoned mortality. People die obviously. That's very important. And harvesting people and relating them to PM10 and ozone, I think it's important. But it's a crude measure.

Morbidity is a lot better. So we want to certainly encourage more and better morbidity studies.

But the other end is morbility. And morbility says serious subclinical disease. And we want data on serious subclinical disease. And it's morbility m-o-r-b-i-l-i-t-y. And morbility is the result of losing lung tissue -- well, in respect to the lung. So every day everybody loses some lung tissue. As you get older, you get shorter. You're losing cells all the time.

The point is: Is that there is a thing called the loss of lung reserves. And there's a slope. And the last word I wanted to say is it would be great if we're all on the slope and it takes us to a hundred years of age. Which says, have enough lung left for the rest of your life. But how many people are on a down slope, including young people.

So I wanted to see the element of judgment, which I felt was short in here, put in. It's very hard. It's very intangible in terms of dollars and cost benefit. But this is a judgmental decision. And I think knowing that there is a problem, knowing there is a disease and knowing that ozone offers us a chance to ameliorate it -- we don't know how much, but it's some, and maybe a lot -- I think we should do it.

CHAIRPERSON KLEINMAN: Thank you.

And actually that leads in very nicely to the next issue, which is: What are the potential benefits of achieving the standard as stated. And so --

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE:

Dr. Kleinman, do you want to take a break right now for the court reporter?

Do you need time?

CHAIRPERSON KLEINMAN: We could do that.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE:

I'm just saying, does the court reporter need a break?

Okay. So maybe just like a five-minute --

CHAIRPERSON KLEINMAN: I think the consensus is, yes, we should take a break.

Let's take --

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE:

-- five minutes.

CHAIRPERSON KLEINMAN: Well, we've got -- yeah, let's give it 15 minutes.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE:

All right.

CHAIRPERSON KLEINMAN: Fifteen-minute break.

(Thereupon a recess was taken.)

CHAIRPERSON KLEINMAN: Okay. We're going to terminate our break and begin the proceedings. I think most of the -- the Committee's in the room at least. They're not all at the table, but they're in the room.

So what I'd like to do is continue on with discussion of the Health Benefits Assessment.

And Lauri Chestnut will lead off.

ADVISORY COMMITTEE MEMBER CHESTNUT: Are we ready to go?

The Health Benefits chapter, I found it interesting that it was -- it's not used in the

standard-setting process and it kind of came after the fact, but it seemed to generate a lot of comments.

And in reviewing the chapter and looking at the comments and the response to comments, most of the comments that I had on -- or suggestions on the analysis that was done have been addressed in the response to comments that came out. So I will -- I thought it might be useful to go through and reinforce which of those things I thought most important to address in the benefits analysis chapter.

And I think one of the things that would help is giving a better context up front or a little more elaboration. And it came out in some of the comments and response to comments about what the intended purpose of this benefit analysis is, because that will help couch what's sufficient to address those -- the issues, since it's not being used to set the standard and it's not being part of -- it's not part of a full cost-benefit analysis, which is often what U.S. EPA is doing with this kind of assessment. But yet it is a lot of useful information about what the implications of meeting these standards would be for the public in California.

So I think it's a useful piece of information. But that's laid out a little bit more.

This is a really challenging analysis to do. And

there's a lot of judgment about which studies we're going to rely on. And making the extrapolations from the literature to numbers is always daunting because it's -- the answers vary depending on which things you select. So there's a lot of room for argument and interpretation. And at some point you just have to hold your nose and jump. And I think -- but I think it's really useful to put some parameters on what do these studies mean in terms of how many cases we might see.

So a lot of the comments on this chapter were about all the reasons why you can't do this and it's so uncertain. But I think that the chapter itself discusses a lot of the limitations and the uncertainties, and you just have to say that and then go ahead and say what the implications are.

The other piece that I think is important in the introduction is to say right up front -- and this came out again in the response to comments -- why the clinical studies are useful for standard setting, but not so useful for doing a comprehensive benefits assessment, and the relationship between that and the kind of exposure assessment that you need to do. There were questions in the comments about "Why aren't you doing a detailed exposure assessment of the population?" and "Shouldn't that be part of the benefit analysis?" I agree with what

the staff did here, that you're doing an epidemiology-based benefit assessment and those studies are using the ambient measurements. So for that assessment you don't need to do the personal exposure kind of assessment.

And, in fact, to do the comprehensive endpoints, mortality, morbidity, the hospitalizations, you can only get -- you can only get a few endpoints if you just look at the clinical studies. So what happened I think the last time -- and I don't know the details of what was done before -- but you should put a lot of resources into a detailed exposure assessment. But the only endpoints that you can quantify from that are the relatively -- the limited group that are measured in the clinical studies -- respiratory symptoms, the lung function changes. So you just don't -- you don't get the comprehensive overview. You really have to look at the epidemiology studies to do that. And to do those you don't need to do the detailed assessment.

Now, a big issue that comes up in the benefits assessment is whether or not there's a threshold, below which you're not going to see any of these health effects. And I think that the -- again, the chapter is appropriate in acknowledging that this literature doesn't really answer that question. But there is some evidence. And in

the interplay between the comments and the response to comments, the staff response included a suggestion of extending the threshold work that was done for one of the endpoints, the emergency room visits, to all the endpoints as a -- basically as a sensitivity test, because you don't really know for sure where that point is.

So the best thing you can do is is do some bounding on, "Well, what if it's here? What if it's here?" And I think it's appropriate, because this hasn't been explored that well in all the studies, to use what evidence there is and say, "Well, what if this applied to all the endpoints?" and then what if it doesn't. So do it both ways. And I think that's -- that's what I understand the response to comments suggested doing.

Along with that, looking at the idea that if you're -- if there's a threshold, that could change the slope of the concentration response function. And I think it's appropriate to look at that. If you -- if there really is a threshold and you've estimated a linear function, you're slope's going to be flatter than if you account for a threshold, and then your effect is beyond that point.

Again, the empirical evidence on this is really uncertain. So you use what's there to try to couch some "what if" approaches to see how much difference it makes.

I'm just looking to see if there's other points on that.

The one thing on the exposures that was also suggested that I think makes some sense is extrapolating from the monitors to -- I think the original was done at the county level -- doing it down to the census track level, I think is a reasonable addition to make. It's something that can be fairly well done -- easily done with the data that are available. It's kind of computationally complex, but the data are there to do that.

And then on the mortality. This is a real difficult issue. In the last rounds of regulatory impact analyses that EPA has done and U.S. EPA for the country, the mortality estimates were still being treated as a sensitivity analysis. But they're on the verge of including it in the total and looking at some recent -- I think the most recent work does push it into the category of "We don't know exactly what the number is, but it's probably not 0," so let's see what the range. And I think the review that's in there is good.

And this -- it's a moving target. There's new publications coming out all the time. You can't keep updating. But perhaps the one that would want to be revisited here is the most recent publication from the NMMAPS data that focused on the ozone results itself. And

I think that this may tilt the central estimate a little bit downward.

But that's something for the staff to evaluate, of how to integrate that into the other pieces. But that's a, you know, big data set from 95 U.S. cities and including 12 that are in California. And I think it's important since they spent a lot more time and it's a new publication that's come out -- they spent a lot more time looking specifically at ozone. And that's about it.

In terms of the study selection, I think that you don't want to just limit to -- as they haven't -- limit to just California studies, that it limits the literature too much. I mean while there are certainly concerns about how is exposure different in California versus other locations, there are so many other uncertainties you want to draw from as large a literature as you can.

But certain endpoints like hospital admissions and emergency room visits that are not just a function of the ambient concentration and the physical response but also the health care system, I think you need to be more cautious about using studies from other countries, because that endpoint might be a really different thing in some locations versus others.

So that's it on my comments on the benefits.

CHAIRPERSON KLEINMAN: Okay. Thank you.

Open up to the rest of the panel. Are there any additional comments?

Does the staff want to make any comment on it?

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: Yeah. I mean some of these comments I'll respond to more I think tomorrow in the official response to comments. But just to clarify, I think everything you said about what we were going to do is right. So we are going to now as a sensitivity a analysis look at both -- we'll look at all the endpoints assuming no threshold and then we'll look at all the endpoints assuming some threshold with some adjustment for the slope.

And I think we're going to be able to draw on a subset of studies to at least get a feeling for what that adjustment of the slope would look like if you presume a threshold on no model that originally did not have a threshold.

And then regarding the exposure assessment, we are going to do another analysis, which will go down to the census track level. Right?

Yeah. So we're going to do for the next go-round rather than at the full county level. So we'll get a better idea. We'll use probably interpolation of three or so monitors and assign that interpolated value using

probably some distance-weighted mechanism to each census track.

And I think that's it. We agree about the mortality. We did use an earlier version of NMMAPS. And as you know, the study that came out last month in the New England Journal with more data, more years of data basically confirmed an association for 95 cities in the U.S.

So they provided two different estimates. One was using a one-day measure and one was using a one-week average of exposure. And using the one-week average the coefficients basically doubled. So we're thinking maybe as to an estimate maybe using some combination of that. And I'll talk about a little bit more tomorrow. But we definitely have incorporated NMMAPS. And we'll try to update it with the newer study as we go through it.

CHAIRPERSON KLEINMAN: Now, that will be strictly for the benefits analysis, not for the --

OEHHA AIR TOXICOLOGY AND EPIDEMIOLOGY SECTION SUPERVISOR OSTRO: Well, I think we'll include a review of the new study in the epi section as well, because it's important enough I think to put in the extra effort to put it in there.

CHAIRPERSON KLEINMAN: Great. Thank you.

Any other comments?

If not, I'm going to, you know, just very briefly -- I think overall the Committee has been very pleased with the quality of the report and the summations. And we've got some specific comments, and we'll go into those a little bit more in detail tomorrow. But at this point I think it would be worthwhile to reserve, you know, the summary comments until we've gotten all of the information presented.

So we have some public representatives who are not able to be here tomorrow. And I thought it would be a good opportunity to give them a few minutes to make their presentations.

So I'm going the turn this back over to Richard and let him moderate this.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE:

Thanks, Dr. Kleinman.

I've gotten a request from two people who said they couldn't be here tomorrow and wanted to make two quick, short statements. And one was Bonnie Holmes-Gen from the Lung Association.

Is she here?

MS. HOLMES-GEN: Good afternoon. I've been sitting too long. I need to stretch out.

I'm Bonnie Holmes-Gen with the American Lung Association of California. And I'm really pleased to be

here and participate in your discussion today.

And I'm here in strong support of the recommendations by the California Air Resources Board staff and OEHHA staff. And I wanted to start off by commending the excellent work that's been done in writing the staff report and the health risk assessment on the proposed new standards.

And I wanted to state up front that we believe these proposed new ozone air quality standards are extremely important to all Californians. These are extremely important because they not only establish the health-based goals that guide the regulatory efforts, but also because they set important national precedent. California has been the leader in terms of air quality and setting air quality standards. And we hope that California will continue to be the leader in having the best science and the standards that are based on the most recent and updated information.

We strongly support the proposed .070 parts per million level proposed for the new eight-hour average standard for ozone. We strongly support retention of a one-hour average standard of .09 parts per million for ozone not to be exceeded. We believe that both these standards are extremely important and neither one can stand alone. Both are needed to provide protection

against short-term peaks as well as longer term exposures that contribute to respiratory irritation and reduction of lung function and the many other health effects that you've discussed today.

I also wanted to state that the American Lung Association was a cosponsor of the legislation, SB 25, by Martha Escutia of 1999 that established this process for review of the air quality standards and air toxic control measures here in California in order to make sure that our State standards protect everyone and especially infants and children.

And partly because of our involvement in that and because of our mission, we are extremely pleased that the Committee has taken charge -- taken its charge to protect children's health very seriously today. Very pleased with the extensive discussion that you've had of children's health issues and the science surrounding health effects in children. And as members have stated today, children are not little adults.

We do need more studies and more information to better understand how pollution is affecting growing and developing lungs in children. And the studies that you have discussed today and that are contained in the staff report raise a lot of alarms: Changed lung architecture in children; premature birth; low birth weights; asthma

exacerbations; and just the tremendous increase -- the increased incidence of asthma in children generally over the past two decades raise a lot of alarms. And we know that we need to do more to protect children, and setting more stringent air quality standards is a big part of that.

Given all this information it seems clear that the only question today from our perspective should be: Are the standards that are being proposed stringent enough? That's seems to us to be the key question that's before you today. That the .0708 hour really should be the upper bound. And the question is whether you should be considering even more stringent standards to better protect children and provide a very clear margin of safety. And I believe you'll probably have that discussion tomorrow, and we look forward to hearing you have that discussion.

In addition to children of course we're concerned about all Californians that are living in unhealthful air. As you know, most Californians are exposed to levels that are at or above the current state standards. And that means millions of Californians are already at risk for impaired lung function, lung irritation, hospital visits, emergency room visits and other problems that are related to smog, including of course premature death.

We're extremely concerned also about the recent research in the Journal of American Medical Association, the landmark study linking ozone exposure to the significant increase in premature death in cities across this country. And that continues to underscore the importance of having a very stringent health standard and moving forward to better protect the public from air pollution, specifically ozone.

We're also concerned about low income communities and communities of color that are disproportionately located in areas that have major sources of air pollution and air toxics, and that unfortunately generally have less access to health care to address pollution -- to address pollution-related illnesses.

The bottom line is: Please take your charge seriously. Your charge is to establish a health-based standard as you know, not to consider whether certain businesses or industries -- or how certain businesses or industries might meet that standard. That's another process. The whole attainment -- the process of determining how attainment is going to be achieved and what specific industries have to do to achieve standards is a whole separate process. And your charge is to establish a health-based goal.

We urge you to move ahead to adopt a stringent

ozone standard for California, at least at the level of .070 parts per million not to be exceeded eight hour and the retention of the one-hour average .09 parts per million standard.

Thank you for your excellent work and for your attention.

CHAIRPERSON KLEINMAN: Thank you.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: Next up was Dr. Harold Farber.

DR. FARBER: I'd like to thank so very much. I thank you for accommodating me today. And thank you for the opportunity to come here to discuss the draft ambient air quality standards for ozone.

I'm Dr. Harold Farber. I'm a pediatric pulmonologist. That's a child lung disease specialist. And author about asthma and a researcher. I'm a founding member of the Solano Asthma Coalition and I'm active with the American Lung Association of the East Bay. I'm here today on behalf of the Health Network for Clean Air, which is a network of statewide health care organizations in California that are involved in air pollution and health issues.

We strongly support the establishment of a new eight-hour average standard for ozone. The 0.070 parts per million level not to be exceeded is clearly needed to

protect public health.

The 6.6 hour chamber studies give clear evidence of adverse effects in healthy young adults at concentrations of 0.08 parts per million. To account for the longer exposures and need to protect sensitive populations, an eight-hour standard of 0.070 parts per million is the highest level that could be considered to provide a margin of safety.

We strongly support the retention of the one-our average standard of 0.09 parts per million ozone not to be exceeded. This standard is necessary to protect against short-term peak concentrations of ozone that are prevalent in California. Studies have demonstrated changes in lung function and adverse respiratory effects in healthy adults as well as increased medication and emergency room use for asthma. From short-term exposures at peak levels it is clear that the one-hour standard of 0.09 parts per million or lower is needed to provide a margin of safety.

Neither the one-hour nor the eight-hour standard can stand alone. Both are needed to provide protection against short-term peaks and long-term exposure that can contribute to respiratory irritation, exacerbate respiratory illness, and reduce lung function.

The not-to-be-exceeded form of the standard is critical to the health protection offered. Standards are

set at levels which will protect public health with an adequate margin of safety. The form of the standard is fundamental to the protection achieved. An alternative form of the standard that allowed multiple days each year when standards could be exceeded would compromise safety.

Public health would not be protected with rounding up conventions that allow concentrations to exceed the level of the standard such as with the federal ozone standards. And, further, multiple exceedances cannot be tolerated due to the public health risk at levels just above the level of the proposed standards.

Research clearly shows that current California ambient air quality standards are not sufficient to protect public health, including sensitive populations, with an adequate margin of safety as required by the Children's Environmental Health Protection Act. Millions of Californians are at risk of impaired lung function, respiratory tract irritation, as well as increased risk for respiratory and cardiovascular hospitalizations and emergency room visits at currently allowable concentrations of ozone.

Children, seniors, people with lung diseases such as asthma and chronic obstructive lung disease, people who work or exercise out doors are especially susceptible to the effects of ozone pollution.

Low income communities and communities of color are disproportionately located in areas with major sources of air pollution. And pollution is taking a disproportionate toll on the health of people living in these communities.

Recent research shows that children growing up in high ozone areas have reduced lung function, the excellent work of the Los Angeles children's health study. And recent research links ozone to premature death. The relationship between mortality and ozone was evident even on days when pollution levels were below the current federal eight-hour standard of 0.08 parts per million.

Closed to 3.3 million school absences per year in California could be avoided if current levels of ozone were reduced to attain the proposed standards according to the California Air Resources Board.

In short, it's important that the proposed 0.070 part per million eight-hour standard not to be exceeded and the 0.09 part per million one-hour standard not to be exceeded be adopted for ozone air pollution control.

Thank you so very much.

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE:

Great. I think that's all the comments we'll do today, because those people couldn't make it tomorrow.

I think also you were given some additional

written comments, is that right, Dr. Kleinman? Is that what you told me?

Actually I'd received some from John Heuss that's going to talk tomorrow. So I'll pass those out to the Committee before they leave.

And then tomorrow morning we'll start with discussion of public comments and staff responses to comments, and we'll take it from there.

CHAIRPERSON KLEINMAN: All right. Sounds good. In that case I believe, unless there are other comments from the Committee, we shall adjourn the meeting until tomorrow morning at --

HEALTH AND EXPOSURE ASSESSMENT BRANCH CHIEF BODE: -- 8:30.

CHAIRPERSON KLEINMAN: -- 8:30.

And this evening, we will meet for dinner in the restaurant down below -- out there at 6.

So enjoy the rest of the afternoon.

(Thereupon the Air Resources Board, Air Quality Advisory Committee meeting recessed at 4:10 p.m.)

CERTIFICATE OF REPORTER

I, JAMES F. PETERS, a Certified Shorthand Reporter of the State of California, and Registered Professional Reporter, do hereby certify:

That I am a disinterested person herein; that the foregoing California Air Resources Board, Air Quality Advisory Committee meeting was reported in shorthand by me, James F. Peters, a Certified Shorthand Reporter of the State of California, and thereafter transcribed into typewriting.

I further certify that I am not of counsel or attorney for any of the parties to said meeting nor in any way interested in the outcome of said meeting.

IN WITNESS WHEREOF, I have hereunto set my hand this 26th day of January, 2005.

JAMES F. PETERS, CSR, RPR
Certified Shorthand Reporter
License No. 10063